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FILE COVERS 1907 - 13 Aug 2002 VOL 137 ISS 7
FILE LAST UPDATED: 12 Aug 2002 (20020812/ED)

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=> d all tot l29

L29 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:540187 HCAPLUS
DN 137:90551
TI Device and method for tracking conditions in an assay
IN **Ellson, Richard N.; Mutz, Mitchell W.; Harris, David L.**
PA USA
SO U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. Ser. No. 751,231.
CODEN: USXXCO
DT Patent
LA English
IC ICM C12Q001-68
ICS B05D003-00; G01N033-53; C12M001-34
NCL 435006000
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 3
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 2002094537	A1	20020718	US 2001-40925	20011228	<--
	US 2002086294	A1	20020704	US 2000-751231	20001229	<--
PRAI	US 2000-751231	A2	20001229	<--		

AB The invention provides a device comprising a substrate having a plurality of different mol. probes attached to a surface thereof and an integrated indicator that exhibits a response when exposed to a condition to which the substrate may be exposed. Each different mol. probe is selected to interact with a different corresponding target, and the indicator response is detectable after removing the indicator from the condition. Alternatively, a substrate is provided having a plurality of mol. probes attached to a surface thereof and a plurality of different integrated indicators. Each indicator is selected to exhibit a response when exposed to one of a plurality of conditions to which the substrate may be exposed. The inventive devices are typically used for biomol., or more

Jan ~~Delaval~~ Delaval

Considered 11/5/02 MCT

Access DB# 72885

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: My-Chau Tran Examiner # : 78933 Date: 8/08/02
Art Unit: 1641 Phone Number 30 5-6999 Serial Number: 09/751,231
Mail Box and Bldg/Room Location: CM1, 8A16 7E12 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Device and Method for Tracking Conditions in an Assay.

Inventors (please provide full names): Richard N. Ellson, Mitchell W. Mutz, David L. Harris

Earliest Priority Filing Date: 12/29/2000

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Mrs. Delaval,

Please perform the following searches:

1) Inventors search

2) Search claims 1, 72, + 80 in which

a) condition = temperature; chemical concentration

b) indicator = fluorescent, magnetic, + electrical

c) probe = nucleotide; peptide; oligonucleotide

Thank-you.

RECEIVED AUG 8 '02 (STIC)

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specifically, nucleotidic assays. The invention also provides for various apparatuses and methods for assaying a sample using the inventive devices.

ST device tracking assay

IT **Sensors**
(Elec. or electrochem.; device and method for tracking conditions in assay)

IT Analysis
(Elec.; device and method for tracking conditions in assay)

IT Information systems
(Electronic; device and method for tracking conditions in assay)

IT **Sensors**
(Interaction; device and method for tracking conditions in assay)

IT Information systems
(Machine-readable; device and method for tracking conditions in assay)

IT **Sensors**
(Magnetic; device and method for tracking conditions in assay)

IT Materials
(Nucleotidic; device and method for tracking conditions in assay)

IT **Laboratory ware**
(Slides; device and method for tracking conditions in assay)

IT Plates
(Well; device and method for tracking conditions in assay)

IT **Analytical apparatus**
Apparatus
Biochemical molecules
Cell
Chemicals
Chemiluminescence spectroscopy
Chemiluminescent substances
Concentration (condition)
Disks
Environment
Evaporation
Fluorescence quenching
Fluorometry
Indicators
Information, biological
Interface
Microarray technology
Molecules
Nucleic acid hybridization
Optical detectors
Reaction
Salinity
Samples
Sensors
Spectroscopy
Temperature
pH
(device and method for tracking conditions in assay)

IT Nucleotides, uses
Oligomers
Peptides, uses
Polymers, uses
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(device and method for tracking conditions in assay)

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(device and method for tracking conditions in assay)

IT **Optical detectors**
(fluorescence; device and method for tracking conditions in assay)

IT Materials

(tapes; device and method for tracking conditions in assay)
IT 75-12-7, Formamide, analysis 7732-18-5, Water, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(device and method for tracking conditions in assay)

L29 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:505297 HCAPLUS
DN 137:43882
TI Integrated device with surface-attached molecular moieties and related machine-readable information
IN **Ellson, Richard N.**; Foote, James K.; **Mutz, Mitchell W.**
PA USA
SO U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U. S. Ser. No. 712,818.
CODEN: USXXCO
DT Patent
LA English
IC ICM C12Q001-68
ICS G06F019-00; G01N033-48; G01N033-50; G06F017-60
NCL 435006000
CC 9-1 (Biochemical Methods)
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002086319	A1	20020704	US 2001-993353	20011113
PRAI	US 2000-712818	A2	20001113		

AB The invention provides a device comprising a substrate having a surface capable of attaching a plurality of mol. moieties, or a surface having a plurality of mol. moieties attached thereto. The substrate also contains machine-readable information relating to the mol. moieties. The information may be contained in a discrete region of the substrate that is non-coplanar with respect to the substrate surface having the plurality of mol. moieties attached thereto. The information may, for example, relate to the identity of the attached mol. moieties or to instructions for attaching the mol. moieties. Also provided are methods and machines for forming and using the devices. More particularly, the invention relates to the formation and use of biomol. arrays on a substrate in conjunction with machine-readable information contained within the same substrate.
ST integrated device surface attached mol machine readable information; biomol array machine readable information
IT Optical memory devices
(DVD players; integrated device with surface-attached mol. moieties and related machine-readable information)
IT Acoustic devices
Apparatus
Coating materials
DNA microarray technology
Disks
Human
Immobilization, molecular
Information systems
Magnetic apparatus
Magnetic disks
Microarray technology
Microtiter plates
Photolithography
Protein microarray technology
(integrated device with surface-attached mol. moieties and related machine-readable information)
IT Phosphorescence
(phosphoimagers; integrated device with surface-attached mol. moieties and related machine-readable information)
IT Bar code labels
Fluorescence

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     Optical ROM disks
        (readers; integrated device with surface-attached mol. moieties and
        related machine-readable information)
IT   Laboratory ware
        (slides; integrated device with surface-attached mol. moieties and
        related machine-readable information)
IT   Information systems
        (storage; integrated device with surface-attached mol. moieties and
        related machine-readable information)
IT   Biochemical molecules
     Molecules
        (surface-attached; integrated device with surface-attached mol.
        moieties and related machine-readable information)
IT   Biopolymers
     Nucleotides, uses
     Oligomers
     Peptides, uses
     RL: ARG (Analytical reagent use); DEV (Device component use); TEM
     (Technical or engineered material use); ANST (Analytical study); USES
     (Uses)
        (surface-attached; integrated device with surface-attached mol.
        moieties and related machine-readable information)
IT   Materials
        (tapes; integrated device with surface-attached mol. moieties and
        related machine-readable information)

L29  ANSWER 3 OF 8  HCAPLUS  COPYRIGHT 2002 ACS
AN   2002:505290  HCAPLUS
DN   137:43881
TI   Device and method for tracking conditions in an assay
IN   Ellson, Richard N.; Mutz, Mitchell W.; Harris,
     David L.
PA   USA
SO   U.S. Pat. Appl. Publ., 20 pp.
     CODEN: USXXCO
DT   Patent
LA   English
IC   ICM  C12Q001-68
     ICS  G01N033-537; C12M001-34
NCL  435006000
CC   9-1 (Biochemical Methods)
     Section cross-reference(s): 3
FAN.CNT 2
     PATENT NO.         KIND  DATE           APPLICATION NO.   DATE
     ---------------    ----  --------       ---------------   --------
PI   US 2002086294       A1   20020704       US 2000-751231    20001229 <--
     WO 2002053777       A2   20020711       WO 2001-US50764   20011228 <--
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2002094537       A1   20020718       US 2001-40925     20011228 <--
PRAI US 2000-751231      A    20001229  <--
AB   The invention provides a device comprising a substrate having a plurality
     of different mol. probes attached to a surface thereof and an integrated
     indicator that exhibits a response when exposed to a condition to which
     the substrate may be exposed.  Each different mol. probe is selected to
     interact with a different corresponding target, and the indicator response
```

is detectable after removing the indicator from the condition. Alternatively, a substrate is provided having a plurality of mol. probes attached to a surface thereof and a plurality of different integrated indicators. Each indicator is selected to exhibit a response when exposed to one of a plurality of conditions to which the substrate may be exposed. The inventive devices are typically used for biomol., or more specifically, nucleotidic assays. The invention also provides for various apparatuses and methods for assaying a sample using the inventive devices.

ST device tracking assay

IT **Sensors**
(Elec.; device and method for tracking conditions in assay)

IT **Optical detectors**
(Fluorescence; device and method for tracking conditions in assay)

IT **Sensors**
(Interaction; device and method for tracking conditions in assay)

IT **Sensors**
(Magnetic; device and method for tracking conditions in assay)

IT Materials
(Nucleotidic; device and method for tracking conditions in assay)

IT Information systems
(data, Electronic; device and method for tracking conditions in assay)

IT Information systems
(data, machine readable; device and method for tracking conditions in assay)

IT **Analytical apparatus**
Biochemical molecules
Cell
Concentration (condition)
Disks
Electrochemical analysis
Environment
Evaporation
Fluorometry
Indicators
Interface
Microarray technology
Molecules
Nucleic acid hybridization
Optical detectors
Plates
Reaction
Salinity
Samples
Spectroscopy
Temperature
Wells
pH
(device and method for tracking conditions in assay)

IT Nucleotides, analysis
Peptides, analysis
RL: ANT (Analyte); ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(device and method for tracking conditions in assay)

IT Oligomers
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(device and method for tracking conditions in assay)

IT Polymers, uses
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(device and method for tracking conditions in assay)

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); DEV (Device component use); ANST

```
     (Analytical study); USES (Uses)
        (device and method for tracking conditions in assay)
IT   Analysis
        (machine; device and method for tracking conditions in assay)
IT   Analysis
        (magnetic; device and method for tracking conditions in assay)
IT   Conveyors
        (slides; device and method for tracking conditions in assay)
IT   Materials
        (tapes; device and method for tracking conditions in assay)
IT   75-12-7, Formamide, analysis   7732-18-5, Water, analysis
     RL: ARU (Analytical role, unclassified); ANST (Analytical study)
        (device and method for tracking conditions in assay)

L29  ANSWER 4 OF 8  HCAPLUS  COPYRIGHT 2002 ACS
AN   2002:450029  HCAPLUS
DN   137:17408
TI   Integrated device with surface-attached molecular moieties and related
     machine-readable information
IN   Ellson, Richard N.; Foote, James K.; Mutz, Mitchell W.
PA   Picoliter Inc., USA
SO   PCT Int. Appl., 50 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  G11B007-24
     ICS  G11B007-00; G11C013-04; G01N033-00; C12Q001-00
CC   9-1 (Biochemical Methods)
FAN.CNT 2
     PATENT NO.       KIND  DATE          APPLICATION NO.  DATE
     ---------------  ----  --------      ---------------  --------
PI   WO 2002047075     A2   20020613      WO 2001-US43810  20011113
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
             UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2000-712818     A     20001113
AB   The invention provides a device comprising a substrate having a surface
     capable of attaching a plurality of moieties, or a surface having a
     plurality of moieties attached thereto.  The substrate also contains
     machine-readable information relating to themoieties.  The information may
     be contained in a discrete regions of the substrate that is non-coplanar
     with respect to the substrate surface having the plurality of moieties
     attached thereto.  The information may, for example, relate to the
     identity of the attached moieties or to instructions for attaching the
     moieties.  Also provided are methods and machines for forming and using
     the devices.  Diagrams describing the app. assembly and operation are
     given.
ST   app biomol nucleotide peptide library imager fluorometry radiochem
IT   Optical memory devices
        (DVD players; integrated device with surface-attached mol. moieties and
        related machine-readable information)
IT   Optical detectors
        (fluorescence; integrated device with surface-attached mol. moieties
        and related machine-readable information)
IT   Analytical apparatus
     Bar code labels
     Biochemical molecules
```

Combinatorial library
Ejectors
Electronics
Fluorometry
Human
Immobilization, molecular
Light
Magnetic disks
Magnetic materials
Microtiter plates
Nucleic acid hybridization
Optical ROM disks
Radiochemical analysis
Sound and Ultrasound
Water reservoirs
(integrated device with surface-attached mol. moieties and related machine-readable information)

IT Nucleotides, analysis
Oligomers
Peptides, analysis
Polymers, analysis
RL: ANT (Analyte); ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(integrated device with surface-attached mol. moieties and related machine-readable information)

IT Imaging
(phospho-; integrated device with surface-attached mol. moieties and related machine-readable information)

IT Microscopes
(slides; integrated device with surface-attached mol. moieties and related machine-readable information)

IT Apparatus
(tapes; integrated device with surface-attached mol. moieties and related machine-readable information)

L29 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:276468 HCAPLUS
DN 136:274241
TI Probe arrays of multifunctional probes containing multiple probe sequences separated by spacers and their preparation using acoustic ejection
IN **Ellson, Richard N.**
PA USA
SO U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 669,267. CODEN: USXXCO
DT Patent
LA English
IC ICM C12Q001-68
ICS C12M001-34; C07H021-04
NCL 435006000
CC 3-1 (Biochemical Genetics)
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002042077	A1	20020411	US 2001-962731	20010924
	WO 2002026756	A2	20020404	WO 2001-US30043	20010925

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2000-669267 A2 20000925
US 2001-962731 A 20010924

AB Probe arrays in which individual members of the array contain sequences hybridizing to any one of several targets that are sepd. by a nonhybridizing spacer segment, i.e., a nucleotide or non-nucleotide segment that has little or no likelihood of binding to an oligonucleotide sequence found in nature are described. Oligonucleotide arrays are also provided in which at least one of the oligonucleotides of the array is a partially nonhybridizing oligonucleotide. The partially nonhybridizing oligonucleotides serve as multifunctional probes wherein each hydrizing segment of a single partially nonhybridizing oligonucleotide serves as an individual probe. Also provided are methods for prepg. and using the partially nonhybridizing oligonucleotides and arrays formed therewith. A particularly preferred method of array fabrication involves the use of focused acoustic energy. Use of a focused acoustic energy device in the prepn. of a probe array on a controlled pore glass surface is demonstrated. Probes were synthesized by phosphoramidite chem. Droplet size and therefore spot size were controlled by controlling the level of acoustic energy. Typical droplet vol. was 0.24 pL with a spot size of 5.6 .mu.m.

ST multifunctional probe array; probe multiple target spacer array prepn; acoustic energy droplet emission probe array synthesis

IT Glass, uses
RL: DEV (Device component use); USES (Uses)
(controlled pore, probe array immobilization on; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

IT Sound and Ultrasound
(focused, for droplet expulsion in prepn. of probe arrays; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

IT Acoustic devices
(for prepn. of probe arrays using focused acoustic energy ejection; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); DEV (Device component use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(multifunctional; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

IT **DNA microarray technology**
(probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

IT 75-05-8, Acetonitrile, uses
RL: MOA (Modifier or additive use); USES (Uses)
(anhyd., in immobilization of oligonucleotides on CPG glass; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

IT 25191-20-2, Oligo(dA) 25609-92-1 25656-92-2 146183-25-7
RL: DEV (Device component use); USES (Uses)
(as spacer; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

IT 2602-34-8, 3-Glycidoxypropyltriethoxysilane 2615-15-8, Hexaethylene glycol
RL: RCT (Reactant); RACT (Reactant or reagent)
(in immobilization of oligonucleotides on CPG glass; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

L29 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:256276 HCAPLUS
DN 136:274212
TI Probe arrays of multifunctional probes containing multiple probe sequences separated by spacers and their preparation using acoustic ejection
IN **Ellson, Richard N.**
PA **Picoliter Inc., USA**
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07H021-00
CC 3-1 (Biochemical Genetics)
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002026756	A2	20020404	WO 2001-US30043	20010925

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 2002042077	A1	20020411	US 2001-962731	20010924
PRAI	US 2000-669267	A	20000925		
	US 2001-962731	A	20010924		

AB Probe arrays in which individual members of the array contain sequences hybridizing to any one of several targets that are sepd. by a nonhybridizing spacer segment, i.e., a nucleotide or non-nucleotide segment that has little or no likelihood of binding to an oligonucleotide sequence found in nature are described. Oligonucleotide arrays are also provided in which at least one of the oligonucleotides of the array is a partially nonhybridizing oligonucleotide. The partially nonhybridizing oligonucleotides serve as multifunctional probes wherein each hydrizing segment of a single partially nonhybridizing oligonucleotide serves as an individual probe. Also provided are methods for prepg. and using the partially nonhybridizing oligonucleotides and arrays formed therewith. A particularly preferred method of array fabrication involves the use of focused acoustic energy. Use of a focused acoustic energy deice in the prepn. of a probe array on a controlled pore glass surface is demonstrated. Probes were synthesized by phosphoramidite chem. Droplet size and therefore spot size were controlled by controlling the level of acoustic energy. Typical droplet vol. was 0.24 pL with a spot size of 5 .mu.m.
ST multifunctional probe array; probe multiple target spacer array prepn; acoustic energy droplet emission probe array synthesis
IT Glass, uses
RL: DEV (Device component use); USES (Uses)
(controlled pore, probe array immobilization on; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)
IT Sound and Ultrasound
(focused, for droplet expulsion in prepn. of probe arrays; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)
IT Acoustic devices
(for prepn. of probe arrays using focused acoustic energy ejection; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)
IT Probes (nucleic acid)

RL: ARG (Analytical reagent use); DEV (Device component use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(multifunctional; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

IT **DNA microarray technology**
(probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

IT 75-05-8, Acetonitrile, uses
RL: MOA (Modifier or additive use); USES (Uses)
(anhyd., in immobilization of oligonucleotides on CPG glass; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

IT 25191-20-2, Oligo(dA) 25609-92-1 25656-92-2 146183-25-7
RL: DEV (Device component use); USES (Uses)
(as spacer; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

IT 2602-34-8, 3-Glycidoxypropyltriethoxysilane 2615-15-8, Hexaethylene glycol
RL: RCT (Reactant); RACT (Reactant or reagent)
(in immobilization of oligonucleotides on CPG glass; probe arrays of multifunctional probes contg. multiple probe sequences sepd. by spacers and their prepn. using acoustic ejection)

L29 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:241258 HCAPLUS
DN 136:275645
TI Focused acoustic energy in the preparation of peptide arrays
IN **Mutz, Mitchell W.; Ellson, Richard N.**
PA USA
SO U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S. Ser. No. 669,997.
CODEN: USXXCO
DT Patent
LA English
IC ICM B05D003-00
ICS C07K014-52; C07K016-00; A61K038-24
NCL 427002110
CC 9-1 (Biochemical Methods)
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002037359	A1	20020328	US 2001-963173	20010925
PRAI	US 2000-669997	A2	20000925		

AB The present invention relates to arrays of peptidic mols. and the prepn. of peptide arrays using focused acoustic energy. The arrays are prepd. by acoustically ejecting peptide-contg. fluid droplets from individual reservoirs towards designated sites on a substrate for attachment thereto. Diagrams describing the app. assembly and operation are given.
ST peptide combinatorial library acoustic energy fluid ejector dispensing app
IT Radiation
(acoustic; focused acoustic energy in prepn. of peptide arrays)
IT Apparatus
(array; focused acoustic energy in prepn. of peptide arrays)
IT Bond
(covalent; focused acoustic energy in prepn. of peptide arrays)
IT Dispensing apparatus
(ejector; focused acoustic energy in prepn. of peptide arrays)
IT Acoustic emission
Analytical apparatus
Combinatorial library
Drops

Immobilization, molecular
PCR (polymerase chain reaction)
Peptide library
Porous materials
Viscosity
Water reservoirs
(focused acoustic energy in prepn. of peptide arrays)
IT DNA
RL: ANT (Analyte); ANST (Analytical study)
(focused acoustic energy in prepn. of peptide arrays)
IT Ligands
Nucleotides, preparation
Oligonucleotides
RL: CPN (Combinatorial preparation); PRP (Properties); CMBI (Combinatorial study); PREP (Preparation)
(focused acoustic energy in prepn. of peptide arrays)
IT Amino acids, reactions
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(focused acoustic energy in prepn. of peptide arrays)
IT Antibodies
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(focused acoustic energy in prepn. of peptide arrays)
IT Antigens
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(focused acoustic energy in prepn. of peptide arrays)
IT Cytokines
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(focused acoustic energy in prepn. of peptide arrays)
IT Enzymes, reactions
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(focused acoustic energy in prepn. of peptide arrays)
IT Kinins (animal hormones)
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(focused acoustic energy in prepn. of peptide arrays)
IT Proteins
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(focused acoustic energy in prepn. of peptide arrays)
IT Lipids, uses
Phospholipids, uses
RL: CUS (Combinatorial use); CMBI (Combinatorial study); USES (Uses)
(focused acoustic energy in prepn. of peptide arrays)
IT Coagulation
(modulators of; focused acoustic energy in prepn. of peptide arrays)
IT Peptides, reactions
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(oligopeptides; focused acoustic energy in prepn. of peptide arrays)
IT Hormones, animal, reactions
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(peptidyl; focused acoustic energy in prepn. of peptide arrays)
IT 9012-90-2
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(Taq; focused acoustic energy in prepn. of peptide arrays)
IT 60118-07-2, Endorphin

RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(focused acoustic energy in prepn. of peptide arrays)

IT 506-68-3, Cyanogen bromide 1648-99-3, Tresyl chloride 6066-82-6, N-Hydroxysuccinimide
RL: CUS (Combinatorial use); CMBI (Combinatorial study); USES (Uses)
(focused acoustic energy in prepn. of peptide arrays)

IT 405350-83-6 405350-84-7
RL: PRP (Properties)
(unclaimed sequence; focused acoustic energy in the prepn. of peptide arrays)

L29 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:240627 HCAPLUS
DN 136:243995
TI Device using focused acoustic energy in the preparation and screening of combinatorial libraries
IN **Ellson, Richard N.**; Foote, James K.; **Mutz, Mitchell W.**
PA **Picoliter Inc., USA**
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM B01J019-00
CC 9-1 (Biochemical Methods)
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002024324	A2	20020328	WO 2001-US30094	20010925

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 2002061258	A1	20020523	US 2000-727392	20001129
	US 2002061598	A1	20020523	US 2001-964193	20010925
PRAI	US 2000-669996	A	20000925		
	US 2000-727392	A	20001129		
	US 2001-964193	A	20010924		

AB The present invention provides a method for the acoustic ejection of fluid droplets from each of a plurality of fluid-contg. reservoirs to prep. combinatorial libraries in the form of microarrays. An acoustic ejection device is used comprised of a plurality of fluid reservoirs, an ejector for generating acoustic radiation and focusing the acoustic radiation generated at a focal point sufficiently near the fluid surface in each of the reservoirs such that a fluid droplet is ejected therefrom toward a site on a substrate surface, and a means for positioning the ejector in acoustically coupled relationship to each of the reservoirs. The combinatorial libraries may comprise biol. or non-biol. moieties. Diagrams describing the app. assembly and operation are given.
ST combinatorial peptide array library acoustic energy app fluid ejector
IT Acoustic emission
Amorphous materials
Apparatus
Biochemical molecules
Combinatorial library
Crystal structure
Drops
Ejectors

Electric potential
Heat
Peptide library
(Device using focused acoustic energy in the prepn. and screening of combinatorial libraries)

IT Ligands
Nucleotides, preparation
Oligonucleotides
Peptides, preparation
RL: CPN (Combinatorial preparation); PRP (Properties); CMBI (Combinatorial study); PREP (Preparation)
(Device using focused acoustic energy in the prepn. and screening of combinatorial libraries)

IT Amino acids, reactions
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(Device using focused acoustic energy in the prepn. and screening of combinatorial libraries)

IT Glass, uses
RL: DEV (Device component use); PRP (Properties); USES (Uses)
(Device using focused acoustic energy in the prepn. and screening of combinatorial libraries)

IT Alloys, properties
RL: PRP (Properties)
(Device using focused acoustic energy in the prepn. and screening of combinatorial libraries)

IT Radiation
(acoustic; Device using focused acoustic energy in the prepn. and screening of combinatorial libraries)

IT Polysaccharides, preparation
RL: CPN (Combinatorial preparation); CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)
(array library of; Device using focused acoustic energy in the prepn. and screening of combinatorial libraries)

IT Apparatus
(arrays; Device using focused acoustic energy in the prepn. and screening of combinatorial libraries)

IT Electron beams
IR radiation
Ions
Light
Photon
UV photoemission
X-ray
(beam of; Device using focused acoustic energy in the prepn. and screening of combinatorial libraries)

IT Temperature
(control of; Device using focused acoustic energy in the prepn. and screening of combinatorial libraries)

IT 50-89-5D, Thymidine, cyanoethylphosphoramidite derivs. 58-61-7D, Adenosine, cyanoethylphosphoramidite derivs. 58-96-8D, Uridine, cyanoethylphosphoramidite derivs. 65-46-3D, Cytidine, cyanoethylphosphoramidite derivs. 118-00-3D, Guanosine, cyanoethylphosphoramidite derivs.
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(Device using focused acoustic energy in the prepn. and screening of combinatorial libraries)

IT 75-05-8, Acetonitrile, uses
RL: CUS (Combinatorial use); PRP (Properties); CMBI (Combinatorial study); USES (Uses)
(anhyd.; Device using focused acoustic energy in the prepn. and

screening of combinatorial libraries)

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=> fil wpix
FILE 'WPIX' ENTERED AT 11:40:45 ON 13 AUG 2002
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FILE LAST UPDATED: 12 AUG 2002            <20020812/UP>
MOST RECENT DERWENT UPDATE          200251   <200251/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> SLART (Simultaneous Left and Right Truncation) is now
    available in the /ABEX field. An additional search field
    /BIX is also provided which comprises both /BI and /ABEX <<<

>>> Implied proximity does currently not work in /BIX
    Searches in this field may be affected <<<

>>> The BATCH option for structure searches has been
    enabled in WPINDEX/WPIDS and WPIX  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

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    http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d all abeq tech abex tot l35

L35  ANSWER 1 OF 5  WPIX (C) 2002 THOMSON DERWENT
AN   2002-471210 [50]   WPIX
CR   2002-403925 [43]; 2002-404916 [43]; 2002-404917 [43]
DNC  C2002-133919
TI   Formation of a combinatorial library of chemical entities on the surface
     of a substrate useful for screening the entities, comprises applying
     focused acoustic energy to reservoirs containing a different chemical
     entity in a fluid.
DC   B04 D16 G05 J04
IN   ELLSON, R N; MUTZ, M W; FOOTE, J K
PA   (ELLS-I) ELLSON R N; (MUTZ-I) MUTZ M W; (PICO-N) PICOLITER INC
CYC  95
PI   WO 2002024324 A2 20020328 (200250)* EN   77p    B01J019-00      <--
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            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
            LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
            SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
     US 2002061598 A1 20020523 (200250)              B01J019-00      <--
ADT  WO 2002024324 A2 WO 2001-US30094 20010925; US 2002061598 A1
     CIP of US 2000-669996 20000925, CIP of US 2000-727392
     20001129, US 2001-964193 20010924
PRAI US 2001-964193    20010924; US 2000-669996    20000925
     ; US 2000-727392    20001129
IC   ICM  B01J019-00
AB   WO 200224324 A UPAB: 20020807
```

NOVELTY - Formation of a combinatorial library of chemical entities on the surface of a substrate involves applying focused acoustic energy (FAE) to several reservoirs containing a different chemical entity in a fluid, where the FAE is applied to eject a droplet from each reservoir toward a site on the surface of the substrate so that a chemical entity is attached in each droplet.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a spatial array (SA) comprising several different ascertainable compositions of matter on a substrate surface divided into several discrete surface sites, where each site contains one ascertainable composition of matter residing in a localized region of the site, and the purity of the composition of matter is uniform along an axis parallel to the substrate surface throughout the localized region and the different sites are present at a density of 1000 - 1500000 (preferably at least 62500, more preferably at least 250000, especially at least 1000000, particularly at least 1500000) sites per square centimeter;

(2) a combinatorial library comprising (SA); and

(3) screening chemical entities to determine the reactivity of each chemical entity toward an applied reagent or to determine the effect of heat on each chemical entity toward an applied reagent, comprising:

(a) preparing a library of the chemical entities;

(b) contacting the attached chemical entities with a reagent to determine the reactivity or exposing the attached chemical entities to heat or to radiation to determine effect of heat or radiation; and

(c) determining whether any reaction has occurred at, at least one site on the surface of the substrate.

USE - The method is used for formation of a combinatorial library of chemical entities on the surface of a substrate. It is used for:

(i) screening chemical entities e.g. a biomolecule (preferably a nucleotide, an oligonucleotide or peptidic molecule), a ligand, an alloy, a crystalline material or an amorphous material (claimed);

(ii) the discovery and evaluation of a composition of matter having useful biological, chemical and/or physical properties;

(iii) screening and characterizing arrayed material, which are useful for various potential properties, especially physical properties of the surface pertinent to the material properties including surface roughness and grain orientation, and functionalization including silanol formation and electron cloud orientation in crystalline silicon surfaces, potential chemical and physical adsorption sites of various molecules, information that may be useful of itself and in predicting potential for catalytic activity.

ADVANTAGE - The method comprises an improved spatially directable fluid ejection method having sufficient droplet ejection accuracy to permit attainment of high density arrays of combinatorial materials made from a diverse group of starting materials without disadvantages of lack of flexibility and uniformity associated with photolithographic techniques or inkjet printing devices effecting droplet ejection through a nozzle. The arrays do not possess the edge and alignment effect of optical and photolithographic masking respectively. Also they are not subjected to imperfect spotting alignment from inkjet nozzle-directed deposition of reagents.

Dwg.0/3

FS CPI

FA AB; DCN

MC CPI: B04-B03B; B04-B03C; B04-E01; B04-N04; B11-C07B2; B11-C08A; B11-C08E6; B11-C09; B12-K04E; D05-H09; D05-H10; G05-F; J04-B01

TECH UPTX: 20020807

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Method: FAE is applied by:

(1) acoustically coupling each reservoir in succession to an ejector; and

(2) activating the ejector to generate acoustic radiation having a focal point sufficiently near the fluid surface to eject a fluid droplet from

the reservoir.
The method involves:
(a) acoustically coupling a first reservoir containing a first chemical entity in the first fluid to an ejector;
(b) activating the ejector to eject a droplet toward a first site on the substrate;
(c) repeating steps (a) and (b) for a second reservoir containing a second chemical in a second fluid to eject a droplet of the second fluid from the second reservoir toward a second site on the substrate surface; and
(d) repeating step (c) with additional reservoirs each containing a chemical entity in a fluid until a droplet has been ejected from each reservoir.
Step (b) results in attachment of the chemical entity in each droplet to the surface of the substrate. The time period between the activation steps is not more than 1 (preferably 0.1, more preferably 0.01, especially 0.001) seconds. The first site and second site are same. The method further involves:
(a) modifying at least one of the attached chemical entities by:
(i) applying an electrical potential or heat,
(ii) directing a beam of photons; or
(iii) exposing the entity to a chemical agent that reacts with it; and
(b) controlling the temperature of the substrate to control the cooling area of the fluid droplets.
Preferred Components: The matter is a molecular, ion, electron, X-ray, ultraviolet, visible light or infrared beam. The ejected fluid is molten having a volume (pL) of 1 - 5 or less than 1 or a metallic composition. The library is a library of alloys having different metallic compositions or an array and each attached chemical entity is an array element. The substrate surface is comprised of a porous material, which is a permeable material.

ABEX
EXAMPLE - No relevant example is given.

L35 ANSWER 2 OF 5 WPIX (C) 2002 THOMSON DERWENT
AN 2002-405041 [43] WPIX
DNC C2002-113770
TI An oligonucleotide (Ogn) array, for conducting a solid-phase hybridization assay, comprises Ogns with alternating hybridizing/non-hybridizing segments.
DC B04 D16
IN **ELLSON, R N**
PA (ELLS-I) ELLSON R N; (PICO-N) **PICOLITER INC**
CYC 95
PI WO 2002026756 A2 20020404 (200243)* EN 33p C07H021-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
US 2002042077 A1 20020411 (200247) C12Q001-68 <--
ADT WO 2002026756 A2 **WO 2001-US30043 20010925**; US 2002042077 A1 **CIP of US 2000-669267 20000925, US 2001-962731 20010924**
PRAI **US 2001-962731 20010924; US 2000-669267 20000925**
IC ICM C07H021-00; C12Q001-68
ICS C07H021-04; C12M001-34
AB WO 200226756 A UPAB: 20020709
NOVELTY - An oligonucleotide (Ogn) array (I), comprising several Ogns attached to a substrate, where at least one of the Ogns is partially non-hybridizing and comprised of two discrete hybridizing segments with a non-hybridizing spacer segment between them, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a substrate with an Ogn attached to its surface through a

covalent or non-covalent bond, where the Ogn is comprised of two discrete hybridizing segments with a non-hybridizing spacer segment between them; and

(2) synthesizing (M1) (I) comprising providing several Ogns and attaching each one to a particular location on the substrate surface.

USE - (I) is useful for conducting a solid-phase hybridization assay, comprising contacting a sample with (I) under hybridizing conditions and detecting any hybridizing events (claimed).

ADVANTAGE - (I) provides a versatile Ogn array where the individual Ogns can be used as multifunctional probes, enhancing the utility of a single array. This improves over previous arrays, where if array probes are used multifunctionally, there is no means of isolating regions where hybridization is desired from regions where it is not.

Dwg.0/2

FS CPI

FA AB; DCN

MC CPI: B04-B03C; B04-E01; B04-E05; B11-C08E5; B12-K04F; D05-H09; D05-H10; D05-H12D1

TECH UPTX: 20020709

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Array: The hybridizing segments are Ogn segments from 8-400, preferably 16-80 nucleotides in length. The non-hybridizing spacers are comprised of a recurring single nucleotide i.e. (A)n, (T)n, (G)n, (C)n or (N)n, where n is 9-50, preferably 9-20, and N is a non-naturally occurring nucleotide or a modified naturally occurring nucleotide. Each Ogn of the array is attached by a covalent or non-covalent bond, or through a linking moiety Each Ogn may be comprised of a partially non-hybridizing Ogn, and each Ogn is different. The Ogns may be arranged in groups, where all Ogns within any one group are different, and each of the Ogn groups is identical. The Ogns are present at a density of 10-250000 per square cm of substrate surface, preferably at least 1000000, more preferably at least 1500000 per square cm of substrate surface. At least one partially non-hybridizing Ogn includes at least one additional hybridizing segment, and where any two hybridizing segments are spaced apart by a non-hybridizing segment. The substrate surface is a porous or a permeable material. The Ogns of the array (which may also be a multilayer array) are of the formula (F1), and the hybridizing segments may be the same or different, and if more than one hybridizing segment is present, the non-hybridizing segments may be the same or different.

SS-(L)m-X1-Y1-X2-(Y2-X3)n (F1)

SS = substrate surface;

L = linking group;

X1-3 = hybridizing oligonucleotide segments;

Y1,2 = non-hybridizing spacer segments;

m = 0 or 1; and

n = an integer from 0-50.

Preferred Method: In M1 the attaching step comprises applying each Ogn to the surface as a droplet, or by applying focused acoustic energy to each of several fluid-containing reservoirs, where each reservoir contains an Ogn. M1 may also comprise successively coupling individual nucleotidic monomers and/or oligonucleotide segments to several support-bound initial nucleotidic monomer, and to provide at least one Ogn with alternating hybridizing/non-hybridizing segments. Each nucleotidic monomer is applied to the substrate surface as with the Ogns described above.

ABEX

WIDER DISCLOSURE - Disclosed are fabricated Ogns, containing one or more partially non-hybridizing Ogns. Also disclosed is an Ogn density on the substrate surface of the array of 1500000-4000000 per square centimeter.

EXAMPLE - No preparative example given.

L35 ANSWER 3 OF 5 WPIX (C) 2002 THOMSON DERWENT

AN 2002-404917 [43] WPIX

CR 2002-403925 [43]; 2002-404916 [43]; 2002-471210 [50]
DNC C2002-113719
TI Generating array of chemical entities on substrate surface by applying focused acoustic energy to reservoirs containing the entities in fluid, using single ejector with acoustic radiation generator and focusing unit.
DC B04 D16
IN **ELLSON, R N**; FOOTE, J K; **MUTZ, M W**
PA (PICO-N) **PICOLITER INC**
CYC 96
PI WO 2002024325 A2 20020328 (200243)* EN 82p B01J019-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
ADT WO 2002024325 A2 WO 2001-US30113 20010925
PRAI **US 2000-727392 20001129; US 2000-669996 20000925 ; US 2000-669997 20000925**
IC ICM B01J019-00
AB WO 200224325 A UPAB: 20020807

NOVELTY - Generating (M) array of chemical entities (CE) on substrate surface (SS), comprising applying focused acoustic energy (AE) to each of a number of reservoirs each containing CE in fluid, is new. AE is applied using single ejector comprising acoustic radiation generator and focusing unit, in a manner effective to eject a droplet from each reservoir toward a site on SS so that CE in each droplet attaches to it.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a device (11) (I) for acoustically ejecting a droplet of fluid from each of a number of fluid reservoirs (13,15), comprising:

(a) a number of reservoirs each adapted to contain a fluid (14,16);

(b) an acoustic ejector (33) comprising an acoustic radiation generator (35) for generating acoustic radiation and a focusing unit (37) for focusing the acoustic radiation generator; and

(c) a unit (43) for positioning the acoustic ejector in acoustic coupling relationship to each of the reservoirs;

(2) a biomolecular array (II) comprising an array of a number of biomolecules on a substrate surface divided into a number of discrete surface sites, each site containing one biomolecule attached to the substrate surface in a localized regions of site, where the biomolecules are present at the density of at least 62500 biomolecules/cm2; and

(3) a peptide array (III) comprised of a number of peptidic molecules each attached through an optional linking moiety to a substrate surface, where none of the peptidic molecules exhibit signs of shear stress and all of the peptidic molecules are intact and attached to a predetermined site on the substrate surface, or the peptide array is comprised of a number of peptidic molecules each attached through an optional linking moiety to a predetermined site on a porous substrate surface at a density of greater than 62500 peptidic molecules/cm2 of the substrate surface.

USE - (M) is useful for generating an array of chemical entities on the surface of a substrate (claimed). (M) is useful in the preparation of biomolecular arrays such as peptide arrays and oligonucleotide arrays.

DESCRIPTION OF DRAWING(S) - The drawing shows a simplified cross-sectional view of a device for acoustically ejecting a droplet of fluid from each of a number of fluid reservoir, comprising first and second reservoirs, an acoustic ejector, and an ejector position unit.

Device 11

Fluid reservoirs 13,15

Fluids 14,16

Acoustic ejector 33

Acoustic radiation generator 35

Focusing unit 37

Ejector positioning unit 43.
Dwg.1/3

FS CPI
FA AB; GI; DCN
MC CPI: B04-B04C; B04-C01; B04-E01; B04-E05; B04-G01; B04-H01; B04-L01; B11-C08; B11-C08E5; B12-K04; B12-K04F; D05-H09; D05-H10; D05-H12D1
TECH UPTX: 20020709

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (M), the focused acoustic energy is applied to each of the number of reservoirs by acoustically coupling each reservoir in succession to the acoustic ejector, and following each acoustic coupling step, activating the ejector to generate acoustic radiation having a focal point sufficiently near the fluid surface to eject a fluid droplet from the reservoir toward a site on the substrate surface. The ejected droplets has a volume in the range of 1-5 pL, preferably less than 1 pL. The chemical entity is a molecule selected from a biomolecule, nucleotide or oligonucleotide. The molecule is peptidic or saccharidic. The peptidic molecule is comprised of 5-10000, preferably 5-1000 amino acids. The peptidic molecule is an oligopeptide, polypeptide or protein, and is selected from enzymes, antibodies, antigens, coagulation modulators, cytokines, endorphins, peptidyl hormones and kinins. Each peptidic molecule is different. (M) involves acoustically coupling a first reservoir containing a first chemical entity in a first fluid to an ejector that produces acoustic radiation, activating the ejector to generate acoustic radiation having a focal point sufficiently near the surface of the first fluid so as to eject its droplet toward a first site on the substrate surface, acoustically coupling a second reservoir containing a second chemical entity in a second fluid to the ejector, activating the ejector to eject a droplet of the second fluid from the second reservoir toward a second site on the substrate surface, and repeating the steps of acoustically coupling the second reservoir and activating the ejector with additional reservoirs each containing a chemical entity in a fluid until a droplet has been ejected from each reservoir, where the activating steps result in attachment of the chemical entity in each droplet to the surface of the substrate. The time period between activation steps is no longer than 1 second, preferably no longer than 0.001 second. The substrate surface is comprised of a porous material such as permeable material, or a nonporous material. The array is prepared at a density of at least 62500, preferably 1500000 array elements/cm2 of the substrate surface. At least two ejected droplets containing a biomolecule capable of covalent or noncovalent binding to another biomolecule, are deposited at the same designated site on the substrate surface. (M) further comprises prior to acoustically coupling the first reservoir, the steps of employing acoustic ejection in order to fill the first reservoir with the first fluid, and modifying the substrate surface. (M) further comprises prior to acoustically coupling the first reservoir, the steps of acoustically coupling the ejector to a modifier reservoir containing a surface modification fluid, and activating the ejector to generate a modifier ejection acoustic wave having a focal point near the surface of the surface modification fluid in order to eject at least one droplet of the surface modification fluid toward the substrate surface for deposition on it at the first designated site. The steps are repeated to deposit a droplet of the surface modification fluid at the second designated site or at all designated sites. The surface modification fluid increases or decreases the surface energy of the substrate surface with respect to each of the ejected fluids. (M) further comprises, before each ejector activation step, measuring the fluid level in the reservoir in acoustically coupled relationship with the ejector, and using the measurement to adjust the intensity of the acoustic radiation needed in each activation step to ensure consistency in droplet size and velocity. (M) further comprises, before each ejector activation step, determining the orientation of the fluid surface in each reservoir in relation to the acoustic radiation generator, and using the measurements to adjust the direction of the focused acoustic radiation required to ensure consistency

in droplet trajectory.
TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Device: (I) is comprised of a single acoustic ejector. Each of the reservoirs is removable from the device. The reservoirs comprise individual wells in a well plate. The reservoirs are arranged in an array. The distance between the centers of any two adjacent reservoirs is less than 1 cm, preferably less than 0.5 mm. The reservoirs are substantially acoustically indistinguishable. (I) comprises 96, preferably 100000-4000000 reservoirs. At least one reservoir is adapted to contain no more than 100, preferably 10 nl of fluid. Each reservoir contains a fluid which contains a biomolecule which is nucleotidic, peptidic, monomeric, oligomeric or polymeric. The biomolecule in each reservoir is different. At least one of the reservoirs contains an aqueous or nonaqueous fluid, where the nonaqueous fluid comprises an organic solvent. The ejector positioning unit is adapted to eject droplets from each reservoir in a predetermined sequence. (I) further comprises a unit for maintaining the fluid in each reservoir at a constant temperature, where the constant temperature is no more than 10, preferably 5 degrees C the melting point of the fluid, a substrate positioning unit for positioning the substrate surface with respect to the ejector, and a cooling unit for lowering the temperature of the substrate surface. The cooling unit is adapted to maintain the substrate surface at a temperature that causes deposited fluid to substantially solidify after contact with the substrate surface.

ABEX

EXAMPLE - Preparation of an array of oligonucleotides in the form of a library, and the use of focused acoustic energy in the solid phase synthesis of oligonucleotides was as follows. Microporous glass, preferably controlled pore size glass (CPG), was sintered onto the surface of a glass plate to form a CPG layer having a thickness sufficient to enable permeation to both the downward flow and the lateral wicking of fluids. Accordingly, the CPG was applied to the glass surface at a thickness of 20 micro-m and the glass with powdered CPG resident on it was heated at 750 degrees C for 20 minutes and then cooled. Commercially available microscope slides were used as supports. Depending on the specific glass substrate and CPG material used, the sintering temperature was adjusted to obtain a permeable and porous layer that was adequately attached to the glass beneath while substantially maintaining the permeability to fluids and thickness of the microporous glass layer. The slides heated for 20 minutes with a 1 cm square patch of microporous glass applied at a pre-heating thickness of 20 micro-m yielded a sintered layer of substantially the same depth as preheating, namely 20 micro-m. The microporous glass layer was derivatized with a long aliphatic linker that can withstand conditions required to deprotect the aromatic heterocyclic bases. The linker, which had a hydroxyl moiety, the starting point for the sequential formation of the oligonucleotide from nucleotide precursors, was synthesized in two steps. First, the sintered microporous glass layer was treated with 25 % solution of 3-glycidoxypropyltriethoxysilane in xylene containing several drops of Hunig's base as a catalyst. The slides were then washed with MeOH, Et2O and air dried. Neat hexaethylene glycol and a trace amount of concentrated H2SO4 acid were added and the mixture was kept at 80 degrees C for 20 hours. The slides were washed with MeOH, Et2O, air dried and stored. Focussed acoustic ejection of 0.24 pL of anhydrous acetonitrile containing a fluorescent marker onto the microporous substrate was then shown to obtain a circular patch of 5.6 micro-m diameter on the permeable sintered microporous glass substrate. The amount of acoustic energy applied at the fluid surface was adjusted to ensure an appropriate diameter of chemical synthesis for the desired site density. 5.6 micro-m diameter circular patches were suitable for preparing an array having a site density of 10 to the power 6 sites/square cm with the circular synthetic patches spaced 10 micro-m apart center to center, and the synthetic patches therefore spaced edge to edge at least 4 micro-m apart at the region of closest proximity. All subsequent spatially directed acoustically ejected volumes were of 0.24 pL. The oligonucleotide

synthesis cycle was performed using a coupling solution prepared by mixing equal volumes of 0.5 M tetrazole in anhydrous acetonitrile with a 0.2 M solution of the required beta-cyanoethylphosphoramidite, e.g. A-beta-cyanoethylphosphoramidite, C-beta-cyanoethylphosphoramidite, G-beta-cyanoethylphosphoramidite, and T (or U)-beta-cyanoethylphosphoramidite. After the synthesis was complete, the oligonucleotide was deprotected in 30 % NH3 for 10 hours at 55 degrees C.

L35 ANSWER 4 OF 5 WPIX (C) 2002 THOMSON DERWENT
AN 2002-404916 [43] WPIX
CR 2002-403925 [43]; 2002-404917 [43]; 2002-471210 [50]
DNC C2002-113718
TI Generating array of molecular moieties on porous substrate surface, involves applying focused acoustic energy using acoustic ejector to reservoirs containing a molecular moiety in a fluid.
DC B04 D16 G05 J04
IN **ELLSON, R N; MUTZ, M W**; FOOTE, J K
PA (ELLS-I) ELLSON R N; (MUTZ-I) MUTZ M W; (PICO-N) **PICOLITER INC**
CYC 95
PI WO 2002024323 A2 20020328 (200243)* EN 62p B01J019-00
  RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
  W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
  US 2002061258 A1 20020523 (200244) B01L003-02 <--
ADT WO 2002024323 A2 WO 2001-US30087 20010925; US 2002061258 A1 **CIP of US 2000-669996 20000925, US 2000-727392 20001129**
PRAI **US 2000-727392 20001129; US 2000-669996 20000925**
IC ICM B01J019-00; B01L003-02
AB WO 200224323 A UPAB: 20020807

NOVELTY - Generating (M) an array of molecular moieties on a porous substrate surface divided into a number of discrete surface sites, comprising applying focused acoustic energy to each of a number of a reservoirs each containing a molecular moiety in a fluid, is new. The focused acoustic energy is applied using an acoustic ejector comprised of an acoustic radiation generator and a focusing unit.

DETAILED DESCRIPTION - Generating (M) an array of molecular moieties on a porous substrate surface divided into a number of discrete surface sites, comprising applying focused acoustic energy to each of a number of a reservoirs each containing a molecular moiety in a fluid, is new. The focused acoustic energy is applied using an acoustic ejector comprised of an acoustic radiation generator and a focusing unit. In (M), the focused acoustic energy is applied in a manner effective to eject a droplet from each reservoir toward the substrate surface such that the molecular moiety in each droplet attaches to a localized region within a different surface site.

An INDEPENDENT CLAIM is also included for a molecular array (I) comprised of a number of different molecular moieties on a porous substrate surface divided into a number of discrete surface sites, each site containing one molecular moiety attached to the substrate surface in a localized region within the site, where the different sites are present at a density of at least 62500 sites/cm2.

USE - (M) is useful for generating an array of molecular moieties on a porous substrate surface divided into a number of discrete surface sites, where the molecular moieties are biomolecules which are nucleotidic or peptidic, or are oligonucleotides or nucleotidic monomers (claimed).

ADVANTAGE - (M) is a unique and highly accurate method for generating molecular arrays of very high density on porous surfaces. In (M), focus acoustic energy is used with very small fluid volumes, on the order of 1 picoliter or less, to prepare high density arrays on substrates having a porous or even a permeable surface. The acoustic ejection enables highly

accurate deposition of extremely small liquid droplets, so that diffusion of a deposited droplet into neighboring cell is not a problem, and ultra-high array densities are achieved with high porosity and permeable surfaces. Porous, permeable surfaces provides substantially more surface area on which to attach molecules within an array, as the biomolecules can penetrate the surface of the substrate and thus can generate a substantially larger sequence/unit of projected area due to the resulting non-planar distribution of the molecules on an within the substrate surface. (M) overcomes a significant disadvantage of the prior art, since prior methods could not constrain the formation or deposition of biomolecules to a small region, due to the inability to localize the synthesis process or to restrict the migration of materials to prevent adjacent spots from diffusing into each other. The accurate placement of extremely small volumes of fluids enables both multistep in situ synthesis on a substrate surface and deposition of an intact molecule within an extraordinarily small zone without the need to mask, pre-active surface sites, or otherwise modify a predetermined region of a surface.
Dwg.0/2

FS CPI
FA AB; DCN
MC CPI: B04-B03C; B04-C01; B04-E01; B04-E05; B11-C08; B11-C08E5; B12-K04; B12-K04F; D05-H09; D05-H10; D05-H12D1
TECH UPTX: 20020709

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (M) molecular moiety is different. A droplet is ejected toward each surface site, so that every surface site has a molecular moiety attached to it. (M) further comprises stepwise synthesis of an oligonucleotide within each surface site by repeated deposition of individual nucleotidic monomers at each site using focused acoustic energy. A porous substrate surface is composed of at least 62500, preferably 1500000 discrete surface sites.
Preferred Array: In (I), the different sites are present at a density of at least 250000, preferably 1500000 sites/cm2.

ABEX

EXAMPLE - Preparation of an array of oligonucleotides in the form of a library, and the use of focused acoustic energy in the solid phase synthesis of oligonucleotides was as follows. Microporous glass, preferably controlled pore size glass (CPG), was sintered onto the surface of a glass plate to form a CPG layer having a thickness sufficient to enable permeation to both the downward flow and the lateral wicking of fluids. Accordingly, the CPG was applied to the glass surface at a thickness of 20 micro-m and the glass with powdered CPG resident on it was heated at 750 degrees C for 20 minutes and then cooled. Commercially available microscope slides were used as supports. Depending on the specific glass substrate and CPG material used, the sintering temperature was adjusted to obtain a permeable and porous layer that was adequately attached to the glass beneath while substantially maintaining the permeability to fluids and thickness of the microporous glass layer. The slides heated for 20 minutes with a 1 cm square patch of microporous glass applied at a pre-heating thickness of 20 micro-m yielded a sintered layer of substantially the same depth as preheating, namely 20 micro-m. The microporous glass layer was derivatized with a long aliphatic linker that can withstand conditions required to deprotect the aromatic heterocyclic bases. The linker, which had a hydroxyl moiety, the starting point for the sequential formation of the oligonucleotide from nucleotide precursors, was synthesized in two steps. First, the sintered microporous glass layer was treated with 25 % solution of 3-glycidoxypropyltriethoxysilane in xylene containing several drops of Hunig's base as a catalyst. The slides were then washed with MeOH, Et2O and air dried. Neat hexaethylene glycol and a trace amount of concentrated H2SO4 acid were then added and the mixture was kept at 80 degrees C for 20 hours. The slides were washed with MeOH, Et2O, air dried and stored. Focussed acoustic ejection of 0.24 pL of anhydrous acetonitrile containing a fluorescent marker onto the microporous substrate was then shown to obtain a circular patch of 5.6

micro-m diameter on the permeable sintered microporous glass substrate. The amount of acoustic energy applied at the fluid surface was adjusted to ensure an appropriate diameter of chemical synthesis for the desired site density. 5.6 micro-m diameter circular patches were suitable for preparing an array having a site density of 106 sites/cm2 with the circular synthetic patches spaced 10 micro-m apart center to center, and the synthetic patches therefore spaced edge to edge at least 4 micro-m apart at the region of closest proximity. All subsequent spatially directed acoustically ejected volumes were 0.24 pL. The oligonucleotide synthesis cycle was performed using a coupling solution prepared by mixing equal volumes of 0.5 M tetrazole in anhydrous acetonitrile with a 0.2 M solution of the required beta-cyanoethylphosphoramidite, e.g. A-beta-cyanoethylphosphoramidite, C-beta-cyanoethylphosphoramidite, G-beta-cyanoethylphosphoramidite, and T (or U)-beta-cyanoethylphosphoramidite. After the synthesis was complete, the oligonucleotide was deprotected in 30 % NH3 for 10 hours at 55 degrees C.

L35 ANSWER 5 OF 5 WPIX (C) 2002 THOMSON DERWENT
AN 2002-403925 [43] WPIX
CR 2002-404916 [43]; 2002-404917 [43]; 2002-471210 [50]
DNN N2002-317026 DNC C2002-113459
TI Preparing peptide array, involves applying focused acoustic energy to reservoirs containing peptidic molecule in fluid, such that a droplet is ejected from each reservoir toward different site on substrate surface.
DC B04 D16 P42
IN **ELLSON, R N; MUTZ, M W**
PA (ELLS-I) ELLSON R N; (MUTZ-I) MUTZ M W
CYC 1
PI US 2002037359 A1 20020328 (200243)* 18p B05D003-00 <--
ADT US 2002037359 A1 **CIP of US 2000-669997 20000925, US 2001-963173 20010925**
PRAI **US 2001-963173 20010925; US 2000-669997 20000925**
IC ICM B05D003-00
ICS A61K038-24; C07K014-52; C07K016-00
AB US2002037359 A UPAB: 20020807
NOVELTY - Preparing (M) an array comprised of a number of peptidic molecules attached to a substrate surface, involves applying focused acoustic energy to each of a number of reservoirs each containing a peptidic molecule in a fluid, where the focused acoustic energy is applied in a manner effective to eject a droplet from each reservoir toward a different site on a substrate surface.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a peptide array (I) comprised of a number of peptidic molecules each attached through an optional linking moiety to a substrate surface, where substantially none of the peptidic molecule exhibits science of shear stress and substantially all of the peptidic molecular are intact and attached to a predetermined site on the substrate surface.

USE - (I) allows for the facile quantitation of antibody titer by determining the number of antibodies that bind to the array from a known sample volume, for establishing relative affinities of ligands to a peptidic molecule, by identifying the number of peptide-bound ligands and comparing the number for each ligand tested, and in high throughput screening applications where a large number of potential ligands are passed over the array. (I) is also useful for screening a particular ligand against a large number of peptide molecules.

ADVANTAGE - The method involves improved acoustic fluid ejection method having sufficient droplet ejection accuracy so as to enable the preparation of high density peptidic arrays without the disadvantages associated with photolithographic techniques or inkjet printing devices relying on a nozzle or relatively large volumes of materials for droplet ejection. Specifically acoustic fluid ejection devices provide improved control over the spatial direction of fluid ejection without the disadvantages of lack of flexibility and uniformity associated with

photolithographic techniques or inkjet printing devices.
DESCRIPTION OF DRAWING(S) - The figure shows the simplified cross-sectional view of the acoustic fluid ejection device.
Dwg.1/2

FS CPI GMPI

FA AB; GI; DCN

MC CPI: B04-B01B; B04-C01; B04-J01; B04-L01; B04-N04; D05-H10; D05-H11

TECH UPTX: 20020709

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: The focused acoustic energy is applied to each of the number of reservoirs by acoustically coupling each reservoir in succession to an ejector that produces acoustic radiation, and following each acoustic coupling step, activating the ejector to generate acoustic radiation having a focal point sufficiently near the fluid surface so as to eject a fluid droplet from the reservoir toward a designated site on the substrate surface. Each peptidic molecule is an oligopeptide, polypeptide or a protein e.g. enzyme, antibody, antigen coagulation modulator, cytokine, endorphin, peptidyl hormone and kinin, comprised of 5-10000, preferably 5-1000 amino acids. Each peptidic molecule is different. Each of the ejected droplets has a volume in the range of 1 pL-5 pL, preferably less than 1 pL. The fluid has a viscosity of at least 40 cP, preferably 1000 cP. (M) further involves acoustically coupling a first reservoir containing a first peptidic molecule in a first fluid to an ejector that produces acoustic radiation, activating the ejector to generate acoustic radiation having a focal point sufficiently near the surface of the first fluid so as to eject a droplet toward a first designated site on the substrate surface, acoustically coupling a second reservoir containing a second peptidic molecule in a second fluid to the ejector, activating the ejector to eject a droplet of the second fluid from the second reservoir toward a second designated site on the substrate surface, and repeating the above said steps with additional reservoirs each containing a peptidic molecule in a fluid until a droplet has been ejected from each reservoir. The time period between the activation steps is no longer than 1 second, preferably no longer than about 0.001 seconds. The activation and the coupling steps results in covalent or non-covalent attachment of the first and second peptidic molecules, respectively, to the first and second designated sites on the substrate surface. The method further involves pretreating the surface substrate with an activating agent e.g. cyanogen bromide, tresyl chloride and N-hydroxysuccinimide. The substrate surface is comprised of a permeable porous material. The array is prepared at a density in the range of 10-250000, preferably 1000000 peptidic molecules, per square cm of the substrate surface.
Preferred Array: (I) comprises a number of peptidic molecules in groups, where all peptidic molecules within any one group are different, and each peptidic molecule group is identical to each other peptidic molecule group. The designated site on the substrate surface includes a lipidic material e.g. phospholipid. At least one of the peptidic molecule within the array is in a lipidic material, and at least one other of the peptidic molecules within the array is in an aqueous fluid.

ABEX

EXAMPLE - Deposition of a peptidic molecule on a substrate using focused acoustic energy does not affect the structure of activity of the molecule. The peptidic molecule employed was TAQ polymerase, a thermostable DNA polymerase. The polymerase was ejected using a focused acoustic energy system from a well plate onto a polypropylene receiving tube using an F=2 lens. The enzymatic activity of the deposited polymerase was then evaluated using a polymerase chain reaction (PCR) assay. For this experiment, TAQ was used to amplify a randomly chosen sequence of the Puc18 vector. The primers used were 5'-AACGTTGTAAAACGACGGCCAGT and 5'-ACGATAGTTACCGGATAAGGCGC at final concentrations of 1.0 microMolar each. The extent of PCR reaction was evaluated by agarose gel electrophoresis stained with ethidium bromide at a concentration of 0.5 micrograms/ml. The intensity of 1 kb DNA product band for TAQ transferred through focused

acoustic ejection was similar to that of the band intensity of non-ejected TAQ. Therefore, it appears that this protein may be subjected to focused acoustic ejection without significant loss of enzymatic activity.

```
=> d his

     (FILE 'HOME' ENTERED AT 11:17:56 ON 13 AUG 2002)
                SET COST OFF

     FILE 'BIOSIS' ENTERED AT 11:18:08 ON 13 AUG 2002
                E PICOLITER/CS
                E PICOLITER
L1           62 S E3-E6
                E ELLSON R/AU
                E MUTZ M/AU
L2            7 S E3,E6,E7
                E HARRIS D/AU
L3          542 S E3,E24
L4           66 S E56,E58
L5            0 S L2 AND L3,L4
L6            0 S L3 AND L4
L7            0 S L1 AND L2-L4
L8          615 S L2-L4
L9            5 S DEVICE AND L8
L10           2 S 01006/CC AND L8

     FILE 'HCAPLUS' ENTERED AT 11:22:41 ON 13 AUG 2002
                E PICOLITER/PA,CS
L11           3 S E3-E6
                E ELLSON R/AU
L12          16 S E4
                E MUTZ M/AU
L13          37 S E3,E9-E11
                E HARRIS D/AU
L14         120 S E3,E24-E26
L15         108 S E73,E74,E93-E96
L16           3 S L11 AND L12-L15
                E WO2001-US50764/AP,PRN
L17           1 S E3
                E US2000-751231/AP,PRN
L18           2 S E3,E4
L19           5 S L16,L17,L18 AND L11-L18
L20        4500 S LABORATORY WARE+NT/CT
L21       10176 S ANALYTICAL APPARATUS+NT/CT
L22       56980 S SENSORS+NT/CT OR BIOSENSORS+NT/CT
L23       20613 S OPTICAL DETECTORS+NT/CT
L24       12994 S INDICATORS+NT/CT
L25         961 S MICROARRAY TECHNOLOGY+NT/CT
                E MICROARRAY TECHNOLOGY+ALL/CT
L26        4257 S E2+NT
L27           7 S L11-L19 AND L20-L26
L28           3 S L27 NOT L19
L29           8 S L19,L27,L28

     FILE 'HCAPLUS' ENTERED AT 11:32:34 ON 13 AUG 2002
                SEL PN APPS L29

     FILE 'WPIX' ENTERED AT 11:33:18 ON 13 AUG 2002
L30           5 S E1-E26
                E WO2001-US50764/AP,PRN
                E US2000-751231/AP,PRN
                E PICOLIT/PA
```

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L31            5 S E4,E5
                 E ELLSON R/AU
L32           40 S E3,E5
                 E MUTZ M/AU
L33           13 S E3,E5
                 E HARRIS D/AU
L34           89 S E3,E15-E17
L35            5 S L30 AND L31-L34

     FILE 'WPIX' ENTERED AT 11:40:45 ON 13 AUG 2002

=> fil wpix
FILE 'WPIX' ENTERED AT 14:29:24 ON 13 AUG 2002
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FILE LAST UPDATED: 12 AUG 2002              <20020812/UP>
MOST RECENT DERWENT UPDATE            200251   <200251/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> SLART (Simultaneous Left and Right Truncation) is now
    available in the /ABEX field. An additional search field
    /BIX is also provided which comprises both /BI and /ABEX <<<

>>> Implied proximity does currently not work in /BIX
    Searches in this field may be affected <<<

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=> d bib abs tech tot

L49  ANSWER 1 OF 97  WPIX (C) 2002 THOMSON DERWENT
AN   2002-470917 [50]   WPIX
DNN  N2002-371772       DNC C2002-133834
TI   Array of molecules for detecting analytes e.g. DNA, RNA or proteins
     present in a sample comprises molecules created on surface of
     substrate with predetermined fenestrations and thickness.
DC   B04 D16 P42 S03
IN   KUMAR, R
PA   (KUMA-I) KUMAR R
CYC  1
PI   US 2002051995 A1 20020502 (200250)*      12p <--
ADT  US 2002051995 A1 Provisional US 2000-244134P 20001030, Provisional US
     2000-251332P 20001206, US 2001-17536 20011029
PRAI US 2001-17536    20011029; US 2000-244134P  20001030;
     US 2000-251332P  20001206
AN   2002-470917 [50]   WPIX
AB   US2002051995 A UPAB: 20020807
     NOVELTY - Array (I) of molecules comprising molecules created on surface
     of substrate with predetermined fenestrations larger than 1 mu m
```

or a thickness of less than 0.5 mm, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) fabricating the above array; and
(2) composite array of molecules comprising two or more of the above arrays stacked together.
USE - (I) is useful for detecting analytes (e.g. deoxyribonucleic acid (DNA), ribonucleic acid (RNA) or proteins) present in a sample, and for sample analysis (claimed).
ADVANTAGE - The target molecules in the sample solution are freely mobile across the **substrate**, and such mobility allows a number of such arrays to be stacked together to fabricate high-density three-dimensional arrays.
DESCRIPTION OF DRAWING(S) - The figure shows the top view of array of molecules.
Solid **substrate**; 10
Fenestrations 14
Molecular array. 16
Dwg.1/9

L49 ANSWER 2 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-464865 [50] WPIX
DNN N2002-366410 DNC C2002-132388
TI Modified biomolecule array useful for detecting e.g. DNA has a modified surface with regular and uniform spots where the biomolecule can attach.
DC B04 D16 **S03**
IN KITSUNAI, T; KONDOH, Y; MATSUMOTO, K; NOJIMA, T; TAKENAKA, S; TASHIRO, H
PA (RIKE) RIKEN KK; (UYWA-N) UNIV WASEDA; (KITS-I) KITSUNAI T; (KOND-I) KONDOH Y; (MATS-I) MATSUMOTO K; (NOJI-I) NOJIMA T; (TAKE-I) TAKENAKA S; (TASH-I) TASHIRO H
CYC 29
PI EP 1208909 A2 20020529 (200250)* EN 11p
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
CA 2363820 A1 20020524 (200250) EN <--
JP 2002153272 A 20020528 (200250) 8p
US 2002081715 A1 20020627 (200250) <--
ADT EP 1208909 A2 EP 2001-127937 20011123; CA 2363820 A1 CA 2001-2363820 20011123; JP 2002153272 A JP 2000-358121 20001124; US 2002081715 A1 US 2001-989986 20011121
PRAI **JP 2000-358121 20001124**
AN 2002-464865 [50] WPIX
AB EP 1208909 A UPAB: 20020807
NOVELTY - A biomolecule microarray support for spotting solutions containing probe biomolecules on the surface and immobilizing the probe biomolecules has small-sized probe biomolecule-attachable spots in a regular arrangement on the support surface.
DETAILED DESCRIPTION - AN INDEPENDENT CLAIM is also included for a method of fabricating the microarray comprising allowing the biomolecule-attachable spots to form only on the specific areas of the support by the photolithography and etching method.
USE - The array is useful for spotting solutions containing probe biomolecules e.g. DNA, RNA, PNA or proteins (claimed).
ADVANTAGE - The array has regularly arranged spots which results in the biomolecules attaching in a predetermined, regular manner. This means the array can be used for quantitative as well as qualitative measurement of biomolecules, unlike prior art arrays which were only suitable for qualitative measurement of biomolecules.
Dwg.0/4
TECH UPTX: 20020807
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Microarray: The spots have a layer of biomolecule-immobilizing agents e.g. avidin, streptavidin, biotin, amino group, carbonyl group, hydroxyl group, succinimide group, maleimide group or thiol group. The support is a glass, silicon, plastic,

gold, gold-plated, silver or silver-plated plate. The preferred array has biomolecule-attachable spots of avidin bound molecules which bind in a single layer to the ends of biotin molecules bound to the surface of the support. The probe biomolecules are biotin-labled and bind to the spots by biotin-avidin binding. The biomolecules bound to the spots are DNA, RNA, PNA or proteins which are preferably labeled.

L49 ANSWER 3 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-453565 [48] WPIX
CR 1997-100216 [09]; 2000-021736 [02]; 2000-611523 [58]; 2000-655615 [63]; 2002-254270 [30]; 2002-442881 [47]
DNN N2002-357665 DNC C2002-128937
TI Detecting target substance or determining effect of test sample on binding interactions between binders, by mediated electrochemistry using labels that react with transition metal mediator complexes in redox reaction.
DC B04 D16 **S03**
IN ECKHARDT, A E; GROELKE, J W; STEWART, D H; THORP, H H
PA (ECKH-I) ECKHARDT A E; (GROE-I) GROELKE J W; (STEW-I) STEWART D H; (THOR-I) THORP H H
CYC 1
PI US 2002037530 A1 20020328 (200248)* 24p <--
ADT US 2002037530 A1 CIP of US 1995-495817 19950627, Div ex US 1996-667338 19960620, Div ex US 1998-179665 19981027, CIP of US 1999-267552 19990312, CIP of US 2000-603217 20000626, Div ex US 2000-722065 20001124, US 2001-991015 20011116
FDT US 2002037530 A1 Div ex US 5871918, Div ex US 6132971, CIP of US 6180346
PRAI **US 2000-722065 20001124; US 1995-495817 19950627 ; US 1996-667338 19960620; US 1998-179665 19981027; US 1999-267552 19990312; US 2000-603217 20000626**; US 2001-991015 20011116
AN 2002-453565 [48] WPIX
CR 1997-100216 [09]; 2000-021736 [02]; 2000-611523 [58]; 2000-655615 [63]; 2002-254270 [30]; 2002-442881 [47]
AB US2002037530 A UPAB: 20020802

NOVELTY - Detecting a target substance (I) in a sample or determining effect of a sample on binding interactions between two binders of a binding pair, by mediated catalytic electrochemistry using labels that react with transition metal mediator complexes in detectable catalytic redox reaction, where labels can be naturally present in or attached directly to binders, target molecule or affinity ligands.

DETAILED DESCRIPTION - Detecting the presence or absence of (I) in a test sample by:

(a) providing an electrode comprising a conductive substrate modified with a non-conductive layer having an immobilized binder (B1) capable of binding (I) and through which layer a transition metal mediator (TMM) can freely move to transfer electrons to the conductive substrate;

(b) contacting the immobilized B1 with the test sample to form a target complex if the target substance is present in the test sample;

(c) contacting B1 or target complex, if present, with another binder (B2) capable of binding (I) and having an endogenous or exogenous label (L1) capable of being oxidized in an oxidation-reduction reaction (ORR1);

(d) contacting the electrode, immobilized B1, and the target complex having B2, if present with a TMM that oxidizes L1 in ORR1 from which there is electron transfer to the TMM resulting in regeneration of the reduced form of the TMM as portion of a catalytic cycle;

(e) detecting the ORR; and

(f) determining the presence or absence of the target substance in the test sample from the detected ORR.

Alternatively, the method comprises:

(i) steps (a) and (b) as described above; and further comprises contacting immobilized B1 with a endogenously or exogenously labeled substance capable of binding with immobilized B1, such that the binding of the labeled substance is inhibited if the target complex is present, and

where the label is L1; contacting the electrode, the immobilized B1, (I), and the labeled substance, if present, with a TMM that oxidizes the L1 in an ORR1; and then carrying out steps (e) and (f);

(ii) step (a) as described above; and further comprises contacting the immobilized B1 with a surrogate target capable of binding with the immobilized B1 to form a target complex, the surrogate target having an endogenous or exogenous L1; contacting the target complex with the test sample, so that labeled surrogate target is displaced from the immobilized binder by (I), if (I) is present in the test sample; contacting the electrode, the immobilized binder, and surrogate target, if present with TMM that oxidizes L1 in an ORR1; and then carrying out steps (e) and (f); or

(iii) providing an electrode comprising a conductive substrate modified with a non-conductive layer having an immobilized (I) or an immobilized surrogate (I), and through which layer a TMM can freely move to transfer electrons to the conductive substrate; contacting the immobilized (I) or immobilized surrogate (I) with the test sample and with an endogenously or exogenously labeled binder that will bind the target substance in the test sample such that (I) in the test sample, if present, competes with the immobilized (I) or the immobilized surrogate (I) for the labeled binder, where the label is L1; contacting the electrode the immobilized (I) or immobilized surrogate (I), and the labeled binder, if present, with a TMM that oxidizes L1 in an ORR1, from which label there is electron transfer to the TMM resulting in regeneration of the reduced form of the TMM as portion of a catalytic cycle; and carrying steps (e) and (f); or

(iv) steps (a), (b), (d), (e) and (f).

Determining the effect of a test sample on the binding interactions between two binders of a binding pair by performing steps (a) and (b), and further contacting the immobilized B1 with an endogenously or exogenously labeled B2 for B1, where the label is capable of being oxidized in an ORR1; and further performing steps (d), (e) and (f).

An INDEPENDENT CLAIM is included for a labeled binder (II) of a binding pair useful for mediated catalytic electrochemistry comprising a binder from proteins, protein fragments, recombinant proteins or its fragments, extracellular matrix proteins, ligands, carbohydrates, steroids, hormones, drugs, drug candidates, immunoglobulins, receptors of eukaryotic, prokaryotic or viral origin and oligonucleotides; and an exogenous peptide label containing one or more modified amino acids capable of being oxidized in an ORR at potentials below those of naturally occurring amino acids.

USE - The method is useful for detecting target substance or determining effect of test sample on binding interactions between binders (claimed).

Dwg.0/6

TECH UPTX: 20020802

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: (I) is preferably from proteins or its fragments, ligands, carbohydrates, drugs, drug candidates and hormones, and B1 is from immunoglobulins, receptors which is preferably of eukaryotic, prokaryotic or viral origin, proteins preferably extracellular matrix protein and oligonucleotides. B2 is preferably labeled with an exogenous label especially an oligonucleotide, where the label is a peptide containing amino acids capable of being oxidized in an ORR1 at approximately at most 0.6 V, in which the TMM is osmium2+(4,4'-dimethyl-2,2'-bipyridine)3.

The non-conductive layer is preferably the immobilized B1, where the layer is from streptavidin, avidin, protein A protein G and antibodies or is preferably a silane molecule covalently attached to the conductive substrate, where the silane molecule is further capable of forming a covalent bond with B1. (I) is In the above method, the test sample and B2 are added to immobilized B1 simultaneously.

Preferred Binder: (II) is preferably an antibody, and the modified amino acids in the peptide label are from derivatives of tyrosine and

tryptophan, more preferably is 5-hydroxytryptophan, 3-aminotyrosine and 3,4-dihydroxyphenylalanine.

L49 ANSWER 4 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-443693 [47] WPIX
DNN N2002-349604 DNC C2002-126211
TI Detecting a target nucleotide sequence in an analyte, for use in e.g. drug discovery, comprises using a set of features having oligophosphodiester probes, and subtracting a background signal from an observed signal.
DC B04 D16 **J04 S03**
IN DELENSTARR, G C; LEFKOWITZ, S M; LUEBKE, K J; OVERMAN, L B; SAMPRAS, N M; SAMPSON, J R; WOLBER, P K
PA (DELE-I) DELENSTARR G C; (LEFK-I) LEFKOWITZ S M; (LUEB-I) LUEBKE K J; (OVER-I) OVERMAN L B; (SAMP-I) SAMPRAS N M; (SAMP-I) SAMPSON J R; (WOLB-I) WOLBER P K
CYC 1
PI US 2002051973 A1 20020502 (200247)* 35p <--
ADT US 2002051973 A1 US 1999-398399 19990917
PRAI **US 1999-398399 19990917**
AN 2002-443693 [47] WPIX
AB US2002051973 A UPAB: 20020725

NOVELTY - Detecting the presence and/or amount of a target nucleotide sequence in an analyte comprising:

(a) contacting an aliquot of an analyte suspected of containing the target sequence with a set of features comprising oligophosphodiester probes; and

(b) subtracting a background signal from an observed signal to determine the presence and/or amount of the target sequence in the analyte.

DETAILED DESCRIPTION - Detecting the presence and/or amount of a target nucleotide sequence in an analyte comprising:

(a) providing an analyte suspected of containing the target sequence;

(b) contacting an aliquot of the analyte suspected of containing the target sequence with a set of features comprising oligophosphodiester probes, where the target sequence is labeled with a detectable label capable of generating a measurable signal, and the features comprise:

(i) hybridization features having hybridization probes that selectively hybridize to the labeled target sequence; and

(ii) background features comprising background probes that do not selectively hybridize to the labeled sequence;

(c) detecting an observed signal, which is an amount of signal generated from contacting the target sequence with the features comprising the oligophosphodiester probes;

(d) detecting a background signal, which is an amount of signal generated from the background features; and

(e) subtracting the background signal from the observed signal to determine the presence and/or amount of the target sequence in the analyte.

INDEPENDENT CLAIMS are also included for the following:

(1) the set of features in (b);

(2) validating a test-background feature comprising test-background probes comprising:

(a) providing an analyte containing a target nucleotide sequence;

(b) contacting an aliquot of the analyte with features comprising oligophosphodiester probes, where the target sequence is labeled with a detectable label capable of generating a measurable sequence, and the features comprise:

(i) hybridization features comprising hybridization probes that selectively hybridize to the target sequence;

(ii) test-background features comprising test-background probes that do not selectively hybridize to the target sequence; and

(iii) standard-background features comprising standard background probes that do not selectively hybridize to the target sequence;

(c) detecting an observed signal, which is an amount of signal generated from contacting the target sequence with the features comprising the oligophosphodiester probes;
(d) detecting a test-background signal, which is an amount of signal generated from the test-background features;
(e) detecting a standard-background signal, which is an amount of signal generated from the standard-background features; and
(f) comparing the amount of test-background signal with the amount of standard-background signal; and
(3) a test kit for detecting the presence and/or amount of a target nucleotide sequence in an analyte comprising a container containing an array of the features of (1).
USE - The method is used to detect the presence and/or amount of a target sequence in an analyte. The method is used for estimating background noise in a nucleic acid hybridization assay and for validating a test-background feature (claimed). The method is useful in chemical, biological medical and diagnostic techniques, and for drug discovery.
ADVANTAGE - The method improves detection and analysis in nucleic acid hybridization assays.
Dwg.0/13

TECH UPTX: 20020725
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The hybridization and background probes are bound to an array surface. The target sequence is directly or indirectly labeled with the detectable label. The signal is detected by colorimetric, fluorimetric, chemiluminescent or bioluminescent techniques. The background probes comprise empirically observed inactive probes, probes forming stable intramolecular structures, short probes, reverse polarity nucleotide analogs, abasic phosphodiesters or modified nucleotidic units. The background probes comprise empirically observed inactive probes that are one of P1 - P14. Alternatively the background probes comprise probes forming stable intramolecular structures (PA - PE) or short probes (Pi - Piv).
Preferred Features: The probes are bound to a surface, preferably an array surface, or are present in solution.
cagaggaagagaatctccgcaagaa (P1)
gaatctccgcaagaaaggggagcct (P2)
cgagctgcccccagggagcactaag (P3)
ccagggagcactaagcgagcactgc (P4)
tgaatgaggccttccaactcaagga (P5)
aaggatgcccaggctgggaaggagc (P6)
aggctgggaaggagccagggggggag (P7)
ggagccagggggggagcagggctcac (P8)
tgggctacactgagcaccaggtggt (P9)
aatatgatgacatcaagaaggtggt (P10)
atccctgagctagacgggaagctca (P11)
aactgtggcgtgatggccgcggggc (P12)
gtgtgaaccatgagaagtatgacaa (P13)
ttcgtcatgggtgtgaaccatgaga (P14)
gctagcgaaagctagc (PA)
gcgagcgaaagcgagc (PB)
gcaggcgaaagcaggc (PC)
gcaggggaaagcaggc (PD)
gcataccgaagcacgc (PE)
aaccatgagaagtatgacaa (Pi)
tgagaagtatgacaa (Pii)
agtatgacaa (Piii)
gacaa (Piv)

L49 ANSWER 5 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-437466 [47] WPIX
DNN N2002-344397 DNC C2002-124422
TI Immobilizing nucleic acid molecules on a **substrate** by treating the **substrate** with atomic oxygen plasma produces immobilize

nucleic acids useful for nanotechnology such as nanoelectronics including wires, biosensors and chips.
DC B04 D16 P42 **S03**
IN FORD, W E; HARNACK, O; WESSELS, J
PA (SONY) SONY INT EURO GMBH; (FORD-I) FORD W E; (HARN-I) HARNACK O; (WESS-I) WESSELS J
CYC 27
PI EP 1207207 A1 20020522 (200247)* EN 8p <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2002091245 A1 20020711 (200248) <--
ADT EP 1207207 A1 EP 2000-125433 20001120; US 2002091245 A1 US 2001-988978 20011119
PRAI **EP 2000-125433 20001120**
AN 2002-437466 [47] WPIX
AB EP 1207207 A UPAB: 20020725
NOVELTY - Immobilizing nucleic acid molecules on a **substrate**, comprising treating the **substrate** with atomic oxygen plasma prior to immobilization, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an immobilized nucleic acid obtained by the novel method.
USE - The immobilized nucleic acid is used in nucleic acid based nanotechnology such as nanoelectronics including wires, biosensors and chips (claimed).
Dwg.0/4
TECH UPTX: 20020725
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The nucleic acid my be DNA, PNA, RNA, CAN, HNA, p-RNA, oligonucleotides, primers, polynucleotides, T-junctions of nucleic acids, and/or domains of non-nucleic acid polymer-nucleic acid block copolymers and may be double stranded or single stranded, natural, modified or artificially generated. The **substrate** is a single crystal surface or amorphous surface, preferably a silicon oxide, glass, an aluminum oxide, sapphire, or a perovskite such as SrTi)3, LaAlO3, NdGaO3 or ZrO2 or their derivative or stabilized and/or doped derivative. The method uses microwave generated oxygen plasma producing atomic oxygen or a mixture of gases containing oxygen. Alternatively, the method uses high voltage generated and/or ultraviolet (UV) light-emitting source generated oxygen plasma producing atomic oxygen or a mixture of gases containing oxygen. The **substrate** is treated with atomic oxygen plasma for 0.1-10 minutes using an oxygen pressure of 0.1-1.0, more preferably 0.2-0.8 mbar. The nucleic acid to be mobilized is preferably in an aqueous solution and the **substrate** is treated with the nucleic acid for at least a few seconds up to 5 minutes, preferably for 1-2 minutes.

L49 ANSWER 6 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-436664 [47] WPIX
DNN N2002-343675 DNC C2002-124227
TI Method for detecting analytes, e.g. for immunoassays, comprises determining binding of analytes to solid phases by independent evaluation of signals from measuring plasmon resonance and impedance.
DC B04 D16 L03 S01 **S03**
IN MIRSKY, V
PA (AFFI-N) AFFINITY BIOSYSTEMS AG
CYC 1
PI DE 10054351 A1 20020516 (200247)* 4p <--
ADT DE 10054351 A1 DE 2000-10054351 20001102
PRAI **DE 2000-10054351 20001102**
AN 2002-436664 [47] WPIX
AB DE 10054351 A UPAB: 20020725
NOVELTY - Method for detecting analytes comprising determining the binding of the analyte to a solid phase by independent evaluation of the signals from measuring plasmon resonance and impedance, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(1) a device for carrying out the method; and
(2) a system comprising several of the devices.
USE - For carrying out immunoassays, nucleic acid hybridization assays and binding assays for high throughput screening of pharmaceuticals.
DESCRIPTION OF DRAWING(S) - The drawing shows a schematic view of a device for detecting analytes in immunoassays, nucleic acid hybridization assays and binding assays.
Laser diode 1
Prism 2
Goniometer 3
Gold layer 13
Ag/AgCl electrode for measuring impedance 14
Dwg.1/1

L49 ANSWER 7 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-381917 [41] WPIX
DNN N2002-298901 DNC C2002-107652
TI Nucleic acid detection sensor includes nucleic acid-chain fixed electrodes, and counter electrode arranged opposite to nucleic acid-chain fixed electrodes.
DC B04 D16 **S03**
IN HASHIMOTO, K; ITSUMI, K; MIYAMOTO, H; SUZUKI, K
PA (TOKE) TOSHIBA KK; (HASH-I) HASHIMOTO K; (ITSU-I) ITSUMI K; (MIYA-I) MIYAMOTO H; (SUZU-I) SUZUKI K
CYC 27
PI US 2002039743 A1 20020404 (200241)* 25p <--
EP 1211507 A2 20020605 (200244) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT US 2002039743 A1 US 2001-961249 20010925; EP 1211507 A2 EP 2001-308139 20010925
PRAI **JP 2000-301516 20000929**
AN 2002-381917 [41] WPIX
AB US2002039743 A UPAB: 20020701
NOVELTY - A nucleic acid detection sensor consists of nucleic acid-chain fixed electrodes (102) where a probe nucleic acid chain is fixed. A counter electrode (101) is arranged opposite to the nucleic acid-chain fixed electrodes. Current flows between the counter electrode and the nucleic acid-chain fixed electrodes.
USE - For detecting whether a target nucleic acid chain in test liquid has a specific base sequence.
ADVANTAGE - The inventive sensor detects many kinds of nucleic acids with high-speed and high-accuracy.
DESCRIPTION OF DRAWING(S) - The figure shows a schematic diagram of the inventive nucleic acid detection sensor.
Counter electrode 101
Nucleic acid-chain fixed electrodes 102
Scanning line 104
Dwg.1/21
TECH UPTX: 20020701
TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Components: The counter electrode is commonly provided to nucleic acid-chain fixed electrodes. It may be provided for each nucleic acid-chain fixed electrode. Each fixed electrode has a flat plane where the probe nucleic acid is fixed, and the counter electrode has a flat plane. The flat plane of each fixed electrode is arranged to face the flat plane of the counter electrode. A reference electrode may be provided for each fixed electrode to make voltage between the fixed electrodes and the counter electrode constant. The fixed and the counter electrodes are comb electrodes and arranged to be mutually engaged. The sensor also includes a first amplifier for inputting signal from the reference electrode or a scanning

line (104), a second amplifier for inputting reference potential to apply predetermined potential to the counter electrode, and a reference resistor connected between an output side of the first amplifier and the reference potential. The fixed electrodes and the counter electrode are arranged to permit a flow of test liquid between them, or the fixed electrodes and the counter electrode are exposed to a test liquid. A current change between the fixed and counter electrodes caused by hybridization of probe nucleic acid and nucleic acid in the test liquid is detected. The current change may be caused by a duplex chain cognitive body, which can be added to the test liquid.

L49 ANSWER 8 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-371884 [40] WPIX
DNC C2002-105240
TI Detecting designated genetic sequence in genomic DNA sample, comprises depositing genomic DNA on substrate, adding labeled probe specific for portion of DNA and detecting signal from labeled probe.
DC B04 D16
IN HODGE, T A
PA (HODG-I) HODGE T A
CYC 95
PI WO 2002020842 A1 20020314 (200240)* EN 126p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001088689 A 20020322 (200251) <--
ADT WO 2002020842 A1 WO 2001-US27404 20010904; AU 2001088689 A AU 2001-88689 20010904
FDT AU 2001088689 A Based on WO 200220842
PRAI US 2001-230371 20010904; **US 2000-230371P 20000906**
AN 2002-371884 [40] WPIX
AB WO 200220842 A UPAB: 20020626
NOVELTY - Detecting (M1) a designated genetic sequence (I) in a sample of genomic DNA, comprising depositing genomic DNA on a substrate, adding at least one labeled probe (P) specific for a portion of (I), and detecting the signal from (P) specific for a portion of (I) to detect (I) in the sample of genomic DNA, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) screening a sample for (I) comprising using M1;

(2) screening genomic DNA for (I) comprising using M1;

(3) an automated apparatus for high volume screening and targeted mutagenesis screening of tissue samples sent by a remote user (RU) to a screening laboratory (SL), comprising a means for transmitting an access request from RU to SL through an electronic communications link (ECL), means for transmitting an access enabling response from SL to RU through ECL with screening parameters, means for transmitting screening parameter selections from RU to SL, means for transmitting the sample from RU to SL, means for isolating genomic DNA from the sample, means for depositing genomic DNA on to a substrate, means for screening genomic DNA, and means for transmitting the data to RU;

(4) a high volume apparatus for screening a tissue sample for modified or mutated genomic DNA according to screening parameter selections made by RU, comprising an automated accessioning station for removing liquid from a first well plate to a second well plate, an isolation station for isolating genomic DNA in the second well plate, an optical standardization station for adjusting DNA concentration in the second well plate, an arraying station for depositing the genomic DNA from the second testing plate onto a substrate, a hybridization station for hybridizing labeled probes that bind to the portions of the genomic DNA, a

detection station for detecting the bound labeled probes, means for making screening parameter selections by RU, RU communicating with the apparatus through ECL, and means for communicating screening results to RU through ECL; and

(5) a system for screening genomic DNA in a sample for a designated genomic DNA sequence, comprising a computer having a processor, memory and web browser, where the computer is adapted to receive the screening parameter selections from RU, and a work station that analyzes samples of genomic DNA for the screening parameter selections, where the workstation includes a microarray imager.

USE - The method is useful for detecting a designated genetic sequence in a sample of genomic DNA (claimed). The method is useful for rapid identification of an organism, whose genome possess specific genetic sequences that exist endogenously or has been modified, mutated or genetically engineered.

ADVANTAGE - The method is more accurate, faster and is a high volume transgenic and targeted mutagenesis screening method. The screening results are provided to a researcher more quickly than by the prior art methods.

Dwg.0/11

TECH UPTX: 20020626

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: (I) is a transgenic insert or a selectable marker comprising a sequence of 795, 1026, 600, 34 or 96 nucleotides fully defined in the specification. (P) has at least two binding regions, one specific to a target genetic sequence and the second specific to an amplification molecule e.g. dendrimer or tyramide. M1 further involves adding a labeled probe specific for a reference genetic sequence (11 sequences of 20 nucleotides fully defined in the specification) to the substrate. The method further involves adding a morphological control (e.g. lambda DNA) with the genomic DNA prior to deposition of genomic DNA on the substrate e.g. glass, plastic or membrane. The substrate is functionalized with a chemical moiety that bonds with the genomic DNA immobilized on the substrate by ultraviolet cross-linking or heating. The substrate is an optically flat glass slide having a sufficient number of aldehyde groups to immobilize genomic DNA. The method further involves comparing (I) with a designated control sample of genomic DNA, by depositing the genomic DNA from the sample and control sample at first and second locations on substrate, respectively, adding (P) to the first and second locations on the substrate, detecting the signal from (P), and comparing the signal to detect (I). The sample is preferably a tissue sample, which is treated with lysis buffer to obtain a cellular debris including genomic DNA, and separating the genomic DNA from the cellular debris using magnetic particles after sonication, and carrying out the above said method. The magnetic particles are 1 micro m iron core carboxylated particles. The genomic DNA fragments are of 100 bp-1 kb in size, preferably 500 base pairs. The lysis buffer is formed from constituents that lyses the sample during overnight transit from RU to SL. A sufficient amount of the lysis buffer is added to the sample and the designated control sample by RU to cover the sample and designated control sample in a well of a well plate. (I) is a knock-out or knock-in DNA. Concentration of DNA is 12.5-500 ng/micro liter, preferably 17-250 ng/micro liter of fluid to facilitate detection of (I). The label used in a direct or indirect label. The method further involves screening a sample of tissue for (I), where the tissue sample including the genomic DNA are sent by RU to SL. The method involves extracting genomic DNA by providing lysis buffer to RU, transmitting the lysed test and control samples to SL, and carrying out the above said process. An access request is transmitted from RU to SL, and access enabling response including screening parameters, is transmitted from laboratory to RU, through ECL. Parameters are selected by RU, transmitted to the laboratory, probes conforming to the selected screening parameters are obtained, the probes are received by the laboratory and used for screening the sample. A data is obtained and transmitted to RU by communication link, e.g. Internet.

L49 ANSWER 9 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-340184 [37] WPIX
CR 1999-095351 [08]; 2001-146289 [15]; 2001-367710 [38]; 2002-017124 [02]; 2002-017125 [02]; 2002-017215 [02]; 2002-194904 [25]; 2002-239225 [29]
DNC C2002-097844
TI Identifying polynucleotide in liquid phase comprises contacting polynucleotides derived from organism with nucleic acid probe labelled with detectable molecule and identifying polynucleotide.
DC A89 B04 D15 D16
IN LAFFERTY, W M; KELLER, M; SHORT, J M
PA (LAFF-I) LAFFERTY W M; (DIVE-N) DIVERSA CORP
CYC 97
PI WO 2002031203 A2 20020418 (200237)* EN 228p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2002048809 A1 20020425 (200245) <--
ADT WO 2002031203 A2 WO 2001-US31806 20011010; US 2002048809 A1 CIP of US 1997-876276 19970616, Cont of US 1998-98206 19980616, CIP of US 1999-444112 19991122, CIP of US 2000-636778 20000811, CIP of US 2000-687219 20001012, US 2001-790321 20010221
PRAI US 2001-309101P 20010731; **US 2000-685432 20001010; US 2000-738871 20001215**; US 2001-790321 20010221; US 2001-894956 20010627; **US 1997-876276 19970616; US 1998-98206 19980616; US 1999-444112 19991122; US 2000-636778 20000811; US 2000-687219 20001012**
AN 2002-340184 [37] WPIX
CR 1999-095351 [08]; 2001-146289 [15]; 2001-367710 [38]; 2002-017124 [02]; 2002-017125 [02]; 2002-017215 [02]; 2002-194904 [25]; 2002-239225 [29]
AB WO 200231203 A UPAB: 20020717
NOVELTY - Identifying a polynucleotide in a liquid phase comprises contacting polynucleotides derived from at least one organism with at least one nucleic acid probe labelled with detectable molecule so that the probe is hybridized to the polynucleotides having complementary sequences and identifying a polynucleotide with an analyzer to detect the detectable molecule.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) identifying a polynucleotide encoding a polypeptide which comprises coencapsulating in a microenvironment a library of clones containing DNA obtained from a mixed population of organisms with a mixture of oligonucleotide probes comprising a detectable label and at least a part of a polynucleotide sequence encoding a polypeptide having a specified bioactivity under conditions and for a time to allow interaction of complementary sequences and identifying clones containing a complement to the oligonucleotide probe encoding the polypeptide by separating clones with an analyzer to detect the detectable label;

(2) high throughput screening of a polynucleotide library for a polynucleotide that encodes a molecule which comprises contacting a library containing clones comprising polynucleotides derived from a mixed population of organisms with oligonucleotides probes labelled with a detectable molecule and separating clones with an analyzer to detect the molecule;

(3) screening for a polynucleotide encoding an activity which comprises:

(a) normalizing polynucleotides obtained from an environmental sample;

(b) generating a library from the polynucleotides;

(c) contacting the library with oligonucleotide probes comprising a

detectable label and at least a part of a polynucleotide sequence encoding a polypeptide having a specified activity to select library clones positive for a sequence and

(d) selecting clones with an analyzer to detect the label;

(4) screening polynucleotides which comprises contacting a library of polynucleotides derived from a mixed population of organisms with a probe oligonucleotide labelled with a fluorescence molecule which fluoresces upon binding of the probe to a target polynucleotide of the library to select library polynucleotides positive for a sequence, separating library members that are positive for the sequence with a fluorescent analyzer to detect fluorescence and expressing the selected polynucleotides to obtain polypeptides;

(5) obtaining an organism from a mixed population of organisms in a sample which comprises encapsulating at least one organism from the sample in a microenvironment, incubating under conditions and for a time to allow the organism to grow or proliferate and sorting the organism by a flow cytometer;

(6) identifying a bioactivity or biomolecule which comprises transferring a library containing clones comprising polynucleotides derived from a mixed population of organisms to a first host cell, contacting the cell with a second host cell containing a detectable reporter molecule in a microenvironment and separating clones with an analyzer to detect the molecule;

(7) identifying a bioactivity or biomolecule which comprises transferring a library containing clones comprising polynucleotides derived from a mixed population of organisms to a first host cell, contacting the cell with a second host cell containing a detectable reporter molecule in a microenvironment and optionally separating clones with an analyzer to detect the molecule;

(8) identifying a bioactivity or biomolecule which comprises transferring the extract of a library containing clones comprising polynucleotides derived from a mixed population of organisms to a first host cell and contacting the extract with a second host cell containing a detectable reporter molecule;

(9) identifying a bioactivity or biomolecule which comprises transferring the extract of a library containing clones comprising polynucleotides derived from a mixed population of organisms through a column, transferring the extract to a first host cell, contacting the extract with a second host cell containing a detectable reporter molecule and measuring the mass spectra of the host cell with the extract;

(10) a sample screening apparatus which comprises an array of capillaries comprising at least one wall defining a lumen for retaining a sample, interstitial material between capillaries and at least one reference indicia formed within the interstitial material;

(11) a capillary for screening a sample which comprises a first wall defining a lumen for retaining the sample and forming a waveguide for propagating detectable signals and a second wall formed of a filtering material for filtering excitation energy to the lumen to excite the sample;

(12) a capillary array for screening samples which comprises capillaries as above;

(13) incubating a bioactivity or biomolecule which comprises introducing a first component into at least a part of a capillary of a capillary array, introducing air into the capillary behind the first component and introducing a second component into the capillary;

(14) incubating a sample which comprises introducing a first liquid labelled with a detectable particle into a capillary of a capillary array, optionally with at least one wall coated with a binding material, submersing one end of the capillary into a fluid bath containing a second liquid and evaporating the first liquid;

(15) incubating a sample which comprises introducing a liquid labelled with a detectable particle into a capillary of a capillary array, introducing paramagnetic beads to the liquid and exposing the capillary

containing the beads to a magnetic field;

(16) recovering a sample from one capillary in an array which comprises determining a coordinate position of a recovery tool, detecting a coordinate location of a capillary containing the sample, correlating, via relative movement between the recovery tool and the capillary containing the sample, the coordinate position of the recovery tool with the location of the capillary and contacting the capillary and recovery tool;

(17) a recovery apparatus which comprises a recovery tool to contact at least one capillary and recover a sample and an ejector, connected with the recovery tool, for ejecting the sample from the tool;

(18) a sample screening apparatus which comprises capillaries in an array, interstitial material and at least one reference indicia formed within the interstitial material, and

(19) enriching a polynucleotide encoding an activity which comprises contacting a mixed population of polynucleotides derived from a mixed population of organisms with at least one nucleic acid probe.

USE - Used for screening for polynucleotides, proteins and small molecules using high throughput of multiple samples.

ADVANTAGE - Rapid sorting and screening of libraries from a mixed population of organisms may be effected.

Dwg.0/23

TECH UPTX: 20020613

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Components: The polynucleotides are from a mixed population of cells. The polynucleotides are in a library, preferably an expression library, especially an environmental expression library. The nucleic acid probe has 15-10000 bases. The detectable molecule is a fluorescent or magnetic molecule. The detectable molecule modulates a magnetic field or the dielectric signature of the clone. The analyzer is a fluorescence activated cell sorting apparatus, a magnetic field sensing device, preferably a Superconducting Quantum Interference Device, a multipole coupling spectroscopy device or flow cytometer.

The organism is from an environmental sample, preferably geothermal fields, hydrothermal fields, acidic soils, sulfotara mud pots, boiling mud pots, pools, hot springs, geysers, marine actinomycetes, metazoan, endosymbionts, ectosymbionts, tropical soil, temperate soil, arid soil, compost piles, manure piles, marine sediments, freshwater sediments, water concentrates, hypersaline sea ice, supercooled sea ice, artic tundras, Sargasso sea, open ocean pelagic, marine snow, microbial mats, whale falls, springs, hydrothermal vents, insect and nematode gut microbial communities, plant endophytes, epiphytic water samples, industrial sites or ex situ enrichments. The environmental sample comprises eukaryotes, prokaryotes, myxobacteria (epothilone), air, water, sediment soil or rock and also contains extremophiles, preferably hyperthermophiles, psychrophiles, halophiles, psychrotrophs, alkalophiles or acidophiles. The organism comprises a microorganism.

The polynucleotide is encapsulated in a microenvironment comprising beads, high temperature agaroses, gel microdroplets, cells, ghost red blood cells, macrophages or liposomes. The detectable molecule is a biotinylated substrate, preferably comprising a spacer connected to a fluorophore structure by a first connector and connected to the bioactivity or biomolecule by a second connector and two groups attached to the fluorophore structure by a connector unit. The fluorophore comprises coumarins, resorufins or xanthenes. The spacer comprises alkanes or oligoethylene glycols. The connector units comprise ether, amine, amide, ester, urea, thiourea or other groups.

The polynucleotide encodes an enzyme, preferably lipases, esterases, proteases, glycosidases, glycosyl transferases, phosphatases, kinases, mono- or di-dioxygenases, haloperoxidases, lignin peroxidases, diarylpropane peroxidases, eposize hydrolases, nitrile hydratases, nitrilases, transaminases, amidases or acylases. The polynucleotide encodes a small molecule. The polynucleotide comprises at least one

operon, preferably encoding a complete or partial metabolic pathway, especially polyketide syntheses.
The reporter system is a bioactive system, preferably C12FDG and also comprising a lipophilic tail, or comprises a detectable label. The reporter system comprises a first test protein linked to a DNA binding group and a second protein linked to a transcriptions activation group. The first and second host cells are prokaryotic or eukaryotic cells. The prokaryotic cell is a bacterial cell and the eukaryotic cell is a mammalian cell.

TECHNOLOGY FOCUS - CHEMICAL ENGINEERING - Preferred Apparatus: Each capillary has an aspect ratio of 10:1-1000:1, preferably 20:1-100:1, especially 40:1-50:1 and a length of 5-100 mm. The lumen of each capillary has an internal diameter of 3-500 (preferably 10-500) mum.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Materials: The reference indicia are made of glass. The second wall is made of extra mural absorption glass which is tuned to filter specific wavelengths of light.

L49 ANSWER 10 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-338220 [37] WPIX
DNC C2002-097193
TI Nucleic acid sieving medium compatible with polymerase chain reaction has low concentrations of polymer e.g. less than 0.5 percent polymer, used in microfluidic device, for performing PCR and nucleic acid separation.
DC A18 A25 A89 B04 D16
IN MEHTA, T B
PA (MEHT-I) MEHTA T B
CYC 1
PI US 2002012971 A1 20020131 (200237)* 14p <--
ADT US 2002012971 A1 Provisional US 2000-190773P 20000320, US 2001-792297 20010223
PRAI **US 2000-190773P 20000320**; US 2001-792297 20010223
AN 2002-338220 [37] WPIX
AB US2002012971 A UPAB: 20020613
NOVELTY - A nucleic acid sieving medium (I), comprising one or more polynucleotides, one or more polymerase chain reaction (PCR) reagents, and a polymer solution which comprises less than about 0.5% of polymer, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a microfluidic device (II) for performing PCR and nucleic acid separations, where the device comprises at least one microscale channel (103), and (I) which is disposed within the at least one microscale channel and comprises a polymer solution comprising less than 0.5 % polymer.
USE - (I) comprising less than 0.5 % polymer, is useful for separating polynucleotides (PCR products, RNA or DNA) which involves allowing the polynucleotides to migrate through the sieving medium, separating the two or more polynucleotides, preferably electrophoretically. The method further involves introducing (I) into a microfluidic channel and allowing the two or more polynucleotides to migrate through the sieving medium in the microfluidic channel. (I) is also useful for performing PCR and separating one or more PCR products which involves mixing one or more PCR reaction components with (I) comprising less than 0.5 % polymer solution, thermocycling the PCR sieving medium to produce one or more PCR products, and separating the one or more PCR products by flowing the one or more PCR products through (I). The method preferably involves mixing PCR reaction components with the sieving media in a microfluidic channel and separating the one or more PCR products electrophoretically by flowing the one or more PCR products through (I) in the microfluidic channel. (All claimed). (I) is thus useful in multistep assays e.g. PCR and subsequent product separation.
ADVANTAGE - (I) is compatible with both nucleic acid separations and

PCR because it provides baseline nucleic acid separation and do not inhibit PCR. The low concentration of the polymer does not inhibit PCR but still provides separation of polynucleotides. The mixture is thus compatible with PCR and also serves as a DNA separation medium. (I) provides a single fluid compatible with nucleic acid separations which can now be carried out with a relatively simple loading or fabrication procedure.

DESCRIPTION OF DRAWING(S) - The drawing shows microfluidic device for performing polymerase chain reaction (PCR) and nucleic acid separation.

Microfluidic channel 103.

Dwg.1/3

TECH UPTX: 20020613

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Sieving Medium: (I) comprises polymer solution comprising less than 0.35 % or less of polymer such as:
(a) acrylamide e.g. linear acrylamide, polyacrylamide, polydimethylacrylamide, or polydimethylacrylamide/coacrylic acid; or
(b) agarose, methyl cellulose, polyethylene oxide, hydroxycellulose, or hydroxy ethyl cellulose.
(I) comprises PCR reagents such as thermostable DNA polymerase, several nucleotides, nucleic acid template, primer which hybridizes to the nucleic acid template, or Mg++. (I) also comprises one or more polynucleotides such as DNA, RNA or PCR products.
Preferred Device: (II) further comprises one or more proteins, nucleic acids, PCR reaction components or PCR products disposed within the at least one microfluidic channel.

L49 ANSWER 11 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-329786 [36] WPIX
CR 2002-292069 [33]
DNN N2002-258817 DNC C2002-095350
TI Identifying and characterizing genes in genomic sequences, especially identifying location of exons, intron-exon boundaries in genome of an organism, by using microarrays to analyze transcriptional state of the genome.
DC B04 D16 T01
IN ALTSCHULER, S J; ARMOUR, C D; SCHERER, S; SHOEMAKER, D D; WU, L F
PA (ALTS-I) ALTSCHULER S J; (ARMO-I) ARMOUR C D; (SCHE-I) SCHERER S; (SHOE-I) SHOEMAKER D D; (WULF-I) WU L F; (ROSE-N) ROSETTA INPHARMATICS INC
CYC 97
PI WO 2002018646 A2 20020307 (200236)* EN 91p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2002045169 A1 20020418 (200236) <--
AU 2001086643 A 20020313 (200249) <--
ADT WO 2002018646 A2 WO 2001-US26274 20010824; US 2002045169 A1 Provisional US 2000-227966P 20000825, US 2001-781814 20010212; AU 2001086643 A AU 2001-86643 20010824
FDT AU 2001086643 A Based on WO 200218646
PRAI US 2001-781814 20010212; **US 2000-227902P 20000825;**
US 2000-227966P 20000825
AN 2002-329786 [36] WPIX
CR 2002-292069 [33]
AB WO 200218646 A UPAB: 20020802
NOVELTY - Identifying (I) exons in the genome of a an organism, involves contacting sample comprising RNAs or nucleic acids (NAs) derived from cell(s) of the species with an array comprising many polynucleotide probes of different nucleotide sequences bound to a solid support, identifying probes to which hybridization of NAs occurs and identifying genomic sequences for each of the identified probe.

DETAILED DESCRIPTION - (I) comprises identifying location of exons (101,102) in a genomic sequence, by:

(a) contacting a sample comprising RNAs or NAs derived from one or more cells of species of organism with an array comprising a positionally-addressable ordered array of polynucleotide probes (104,105) bound to a solid support, where the probes comprise at least 100 polynucleotide probes of different nucleotide sequences, each comprising a sequence complementary and hybridizable to a different genomic sequence of the same species of organisms, the respective genomic sequence for the probes being found at sequential sites in the genome of the species of organism, and contacting being under conditions conducive to hybridization between the RNAs or NA and the probes;

(b) identifying one or more probes to which hybridization of one or more of the RNAs or NAs derived from them occurs; and

(c) identifying the genomic sequences for each of the identified probe as the location of an exon within the genome of the species of organism.

INDEPENDENT CLAIMS are also included for the following:

(1) an array (II) comprising a positionally-addressable ordered array of polynucleotide probes as above, where two or more of the probes are complementary and hybridizable to intron sequences of 10 different genes;

(2) a computer-implemented method for designing probes for an array;

(3) a computer system for identifying:

(a) the location of exons within the genome of a species of organism; or

(b) an intron-exon junction boundary in the genome of a species of organism;

(4) a computer program product for identifying:

(a) the location of exons within the genome of a species of organism; or

(b) an intron-exon junction boundary in the genome of a species of organism, for use in conjunction with a computer having a memory and a processor, the computer program product comprising a computer readable storage medium having a computer program mechanism encoded on it; and

(5) preparing (II) by synthesizing several polynucleotide probes on a solid support.

USE - (I) is useful for identifying the location of exons within the genome of a species of organisms including eukaryote, human, plant, or mammal. Once the locations of the exons are determined, the method can be used to identify the approximate location of an intron-exon boundary in the genome of a species of organism. (II) is useful for determining the amino-terminus of a protein, for determining the probability that an individual nucleotide within the genome of a species of organism is expressed, preferably in response to a condition and also for determining whether respective sequences encoded by two or more exons are indicated to be present in a single mRNA transcript (claimed).

Computer system or the computer program product are useful to carry out the above analytical methods.

ADVANTAGE - (I) determines the structure of the gene rapidly, even if the exons are widely separated in the genome or the gene is expressed at low levels. (I) allows for the efficient identification of small genes, genes that do not encode proteins, genes that are transcribed at low levels, and untranslated regions of mRNAs encoding proteins. Accurate gene structure is readily ascertained. (II) enable an efficient and comprehensive genome scan that provided much more detailed data than conventional methods. (II) also allows the structure of the gene to be determined at the same time as the gene is detected, even if the gene is spread over large regions of the genome.

DESCRIPTION OF DRAWING(S) - The figure shows the strategy used to discover exons in a genomic sequence.

Exons 101, 102

Probes 104, 105

Dwg.1/15

TECH UPTX: 20020610
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Array: (II) has in the range of 150-1000, 1000-10000, 10000-50000 or greater than 50000 different polynucleotide probes/cm2. The nucleotide sequences of the probes consists not more than 1000 nucleotides, preferably consists of 10-200, 80-120, or more preferably 60 nucleotides. The genomic sequences for different probes are overlapping in the genome from 10-50% of the length of each of the different probe, or are adjacent in the genome. The genomic sequence for each probe is spaced apart from that of other probes in the genome by less than 200 bp. The distance between 5' ends of the sequential sites is always less than 500 bp and the genomic sequences for the probes span a genomic region of at least 25000 bp. Two or more of the probes are complementary and hybridizable to sequences contained entirely within an intron or the intron sequences of 10 different genes, and the ordered array does not comprise a second set of polynucleotide probes that do not comprise a sequence complementary and hybridizable to the genome of the species of organism. The second set of probes is equal or greater number than the first set of probes. The probes comprising sequences corresponding to repetitive elements, simple repeats or polyA repeats are excluded as probes.
Preferred Method: RNAs or NAs derived from several different cells of the species of organism are contacted with the array. The polynucleotide probes further comprise several polynucleotide probes comprising a sequence complementary and hybridizable to the first set of probes, and identification involves using a hybridization signal generated in the contacting step from the second set of probes to filter a hybridizations signal generated in the contacting step from the first set of probes. The sample comprises RNAs or NAs derived from a first cell or cells of a first tissue type or of a first condition, and a second cell or cells of a second tissue type different from the first tissue type or of a second condition different from the first condition. Hybridization signal generated from the first cell is compared to the signal generated from the second cell. Several probes are tiled across an area predicted to contain or known to contain, exons. The probes include known expressed sequence tags (ESTs) or predicted exons. The method further comprises a sample comprising a labeled population of cellular RNA (mRNA) or NA on the surface of the solid support such that the sample is in contact with polynucleotide probes, such that hybridization occurs between the population and the probes. The population preferably comprises nucleic acids of 1000 different sequences.

L49 ANSWER 12 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-328525 [36] WPIX
CR 2002-225941 [17]; 2002-339267 [17]
DNN N2002-257793 DNC C2002-094840
TI Thermal gradient apparatus used for analysis of biological macromolecules, comprises semiconducting wafer, two adjacent electrical connectors, and power source.
DC A89 B04 D16 **S03**
IN BLUMENFELD, M; CIBUZAR, G T; FISHER, M; NESS, B G V; WILLIAMSON, F
PA (BLUM-I) BLUMENFELD M; (CIBU-I) CIBUZAR G T; (FISH-I) FISHER M; (NESS-I) NESS B G V; (WILL-I) WILLIAMSON F
CYC 1
PI US 2002015996 A1 20020207 (200236)* 45p <--
ADT US 2002015996 A1 Div ex US 2000-630172 20000801, US 2001-853964 20010511
PRAI **US 2000-630172 20000801**; US 2001-853964 20010511
AN 2002-328525 [36] WPIX
CR 2002-225941 [17]; 2002-339267 [17]
AB US2002015996 A UPAB: 20020613
NOVELTY - A thermal gradient apparatus comprising a semiconducting wafer, two adjacent electrical connectors on the wafer, and a power source, where each of the connectors are attached to the wafer at an attachment site, a gap is disposed between the two attachment sites and a power source is

connected to the wafer through the electrical connectors, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) generating a temperature gradient comprising the thermal gradient apparatus;

(2) analyzing biological macromolecules comprising establishing a temperature gradient on a semiconducting wafer having a stratum disposed on it, where the stratum has one or more samples comprising biological macromolecules in thermal contact with the temperature gradient and evaluating the samples to determine thermal stability of the complexes formed with the biological macromolecules in the samples, where the samples are evaluated by measuring a property of the sample;

(3) conducting nucleic acid hybridization comprising establishing a temperature gradient on a semiconducting wafer having a stratum disposed on it, where the stratum has one or more samples comprising nucleic acid molecules in thermal contact with the temperature gradient and performing a hybridization protocol on the samples to determine temperature effect based on the gradient; and

(4) assessing binding complex interactions comprising establishing a temperature gradient on a semiconducting wafer having a stratum disposed on it, where the stratum has one or more samples comprising members of binding complexes in thermal contact with the temperature gradient and evaluating the samples to determine thermal stability of the binding complex on the stratum.

USE - For use in generating temperature gradient useful for the analysis of molecules, preferably biological macromolecules.

ADVANTAGE - The inventive apparatus is able to generate stable temperature gradient.

DESCRIPTION OF DRAWING(S) - The figure is a schematic diagram of the thermal gradient apparatus.

Semiconducting wafer 110
Electrical connectors 114a, 114b
Electrical wires 116a, 116b
Electrical transformer 120
Power source 126
Temperature sensor 130
Gap 134
Temperature controller 136
Relay switch 140
Dwg.1/11

TECH UPTX: 20020610

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Components: The semiconducting wafer is of rectangular shape, and has clipped corners. Both attachment sites are located near the rectangular edges. The two attachment sites are spaced at a distance of 2-180 mm. A temperature gradient formed on the wafer is perpendicular to an attachment line derived from connecting the two attachment sites. The electric connectors and the power source are connected by electrical wires. The thermal gradient apparatus further comprises control circuitry provided between the wafer and the power source. The control circuitry comprises a temperature sensor disposed in the gap and connected to a temperature controller, and an electrical transformer connected in series between the power source and the electrical connectors. A feedback control is provided between the temperature sensor and the temperature controller to maintain the measurement of the temperature sensor within a selected range. The feedback control opens or closes a relay switch. Stratum are disposed in wafer, and consist of DNA chip, protein chip, fluidic cell, microscopic slide, liquid, coverslip, and/or acrylamide gel. The stratum are provided with samples of molecules, labeled probes, or members of a binding complex. The stratum are made of glass, silicon, or plastic.
Preferred Method: The temperature gradient is generated by thermoelectric Peltier device, and formed at 0.1-1 (preferably 0.25-0.7) degrees C/mm.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Components: The semiconducting wafer is a silicon wafer comprising a doping agent consisting of boron, phosphorus, or arsenic.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The samples of molecules consist of nucleic acid molecules, polypeptides, carbohydrates, lipids, hormones, and/or drugs. The labeled probes are fluorescent labeled probes, chemiluminescent labeled probes, or radiolabeled probes. The polypeptides consist of antigens, antibodies, enzymes, receptors, or its fragments. The binding complex comprises nucleic acid duplex, polypeptides, nucleic acid:polypeptide complex, nucleic acid:drug complex, antigen:antibody complex, receptor:drug complex, lipid:polypeptide complex, or carbohydrate:polypeptide complex.

L49 ANSWER 13 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-303419 [34] WPIX
DNC C2002-088222
TI Apparatus for measuring the genetic sequence of electrically charged biopolymers such as RNA, and peptide nucleic acid, has container containing a biopolymer and electrodes electrically insulated from the container.
DC B04 D16
IN TANAAMI, T
PA (YOKG) YOKOGAWA ELECTRIC CORP; (YOKG) YOKOGAWA DENKI KK; (TANA-I) TANAAMI T
CYC 28
PI US 2002028502 A1 20020307 (200234)* 8p <--
EP 1186670 A2 20020313 (200234) EN <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2002085095 A 20020326 (200236) 5p <--
ADT US 2002028502 A1 US 2001-927049 20010809; EP 1186670 A2 EP 2001-120879 20010830; JP 2002085095 A JP 2000-271357 20000907
PRAI **JP 2000-271357 20000907**
AN 2002-303419 [34] WPIX
AB US2002028502 A UPAB: 20020528
NOVELTY - An apparatus for measuring the genetic sequence of electrically charged biopolymers by hybridization, has a container that contains a biopolymer, which can be removed from the apparatus, and an electrode (1) that applies an electric field to the container and are electrically insulated from the container.

USE - The apparatus is useful for measuring the genetic sequence of electrically charged biopolymers such as RNA, peptide nucleic acid (PNA), or electrically charged protein molecules (claimed).

ADVANTAGE - The apparatus is inexpensive and highly reliable. When electric fields are applied to the container, suspended biopolymeric molecules are attracted toward the positive electrode, which increases the speed of hybridization. The container requires neither electrodes nor electrical connection terminals and is therefore inexpensive. A reading unit used with the container requires not more than one pair of an electrode structure and processing circuitry. Thus, the system as a whole is also inexpensive. Since the container has no electrode structure electro-chemical noise or fluctuations are very unlikely and failures due to defective electrical contact with the terminals of the reading unit will never occur. The apparatus requires neither electrodes nor their electrical taps to be formed on the container, which reduces the size of the container. The reading unit can also be downsized since the unit requires not more than one pair of an electrode structure and voltage source circuitry.

DESCRIPTION OF DRAWING(S) - The figure explains how DNA segments are attracted toward an electrode.
Electrode 1
Known DNA segment 2

Unknown DNA segment 3
Dwg.1a/7

TECH UPTX: 20020528
TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Device: The container is made of a film. The electrodes are transparent, made of indium tin oxide (ITO) film and are provided with protrusions formed at spatial positions corresponding to sites where several types of biopolymeric molecules within the container gather. The electrodes are in mechanical contact with the container. Conductive members are formed at spatial positions corresponding to the sites where the biopolymeric molecules within the container gather. The apparatus further comprises a unit for altering the direction of an electric field so that wrongly hybridized segment pairs are separated.

L49 ANSWER 14 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-291233 [33] WPIX
CR 1996-518698 [51]; 2000-125574 [11]; 2000-194332 [12]
DNN N2002-227385 DNC C2002-085376
TI Integrated apparatus, useful for biological research, comprises mechanisms for electrophoretic separation of biopolymer fragment samples, stimulating light emissions and resolution of light emissions into spatial/spectral components.
DC A89 B04 D16 **S03** S05 T01
IN ROTHBERG, J M; SIMPSON, J W; WENT, G T
PA (CURA-N) CURAGEN CORP
CYC 1
PI US 2002009741 A1 20020124 (200233)* 41p <--
ADT US 2002009741 A1 Div ex US 1995-438231 19950509, Cont of US 1999-300163 19990426, US 2001-836383 20010417
FDT US 2002009741 A1 Div ex US 6017434, Cont of US 6218121
PRAI **US 1995-438231 19950509; US 1999-300163 19990426** ; US 2001-836383 20010417
AN 2002-291233 [33] WPIX
CR 1996-518698 [51]; 2000-125574 [11]; 2000-194332 [12]
AB US2002009741 A UPAB: 20020524
NOVELTY - An integrated apparatus for concurrent preparation and analysis of biopolymer fragment samples comprising means for:
(a) preparing biopolymer fragment samples;
(b) holding biopolymer fragment samples into an electrophoretic separation medium;
(c) concurrent electrophoretic separation;
(d) simultaneously stimulating light emissions from fragment; and
(e) simultaneous resolution of light emissions into spatial and spectral components, is new.
DETAILED DESCRIPTION - An integrated apparatus comprising:
(a) a mechanism for preparing from an input biopolymer sample comprising fragments obtained from biopolymer(s) for subsequent analysis;
(b) a mechanism for holding biopolymer fragment samples into an electrophoretic separation medium;
(c) a mechanism for substantially concurrent electrophoretic separation of each of the biopolymer fragment samples loaded into the electrophoretic separation medium;
(d) a mechanism for substantially simultaneously stimulating light emissions from fragments in biopolymer fragment samples; and
(e) a mechanism for substantially simultaneous resolution of the light emissions into spatial and spectral components and generation of output signals, is new.
INDEPENDENT CLAIMS are also included for the following:
(1) generating DNA sequence reaction fragments in one reaction chamber without an intermediate separation step comprising:
(a) performing a polymerase chain reaction amplification with deoxyuridine triphosphate (dUTP) rich polymerase chain reaction (PCR) primers;

(b) fragmenting the dUTP primers with Uracil DNA Glycosylase into fragments ineffective as DNA polymerase primers; and

(c) performing the Sanger sequencing reactions; and

(2) determining DNA samples using spectral signals obtained by spectrographic observation of electrophoretically separated labeled DNA fragments produced by Sanger sequencing reactions, comprising:

(a) cumulating the spectrographic signals into spatial samples representative of fragments of one DNA sample;

(b) comparing the time behavior of the spectral samples with a set of prototype signal time behaviors and selecting prototypes from the set that most closely match the spectral samples; and

(c) outputting the identities of the selected prototypes.

USE - For concurrent preparation and analysis of biopolymer fragment samples, useful for biological research, e.g. Human Genome Project, biotechnology industry, and clinical diagnosis.

ADVANTAGE - The inventive integrated apparatus allows rapid, concurrent generation and analysis of large number of biopolymer fragment samples.

DESCRIPTION OF DRAWING(S) - The figure shows an overall view of the apparatus.

Spectrograph 100
Channels 115
Dwg.1/19

TECH UPTX: 20020524

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Component: The mechanism for substantially concurrent electrophoretic separation is an electrophoretic module comprising flat bottom and top plates. The mechanism for simultaneous resolution of each light emissions is a transmission imaging spectrograph.

Preferred Apparatus: The apparatus further comprises:
(1) a mechanism for the analysis of the detected light emission to give information on the identity of the biopolymer samples;
(2) a mechanism for thermal control for maintaining a selected uniform temperature in the bottom plate;
(3) cross-lane grooves forming cross-lane connecting channels that hold separation medium;
(4) electrodes that causes fragment migration through the connecting channels upon being energized with voltage;
(5) a mechanism for trimming from the output identities of the DNA samples known DNA sequences in the DNA sample;
(6) a mechanism for proofreading in a Monte Carlo manner the trimmed DNA sequences; and
(7) a mechanism for outputting the improved sequence as the DNA sequences of the DNA samples.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Component: The biopolymer fragment samples are DNA sequencing reaction fragment samples labeled with dyes, each having distinctive spectral properties.

TECHNOLOGY FOCUS - POLYMERS - Preferred Material: The separation medium comprises small spheres of an inert material, i.e. polystyrene.

L49 ANSWER 15 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-280951 [32] WPIX
DNC C2002-082700
TI Novel three dimensional internal and external probe carrier for binding a target molecule to a probe, has discrete through well/pillar having an elongated bore/core and defined by interior/exterior.
DC B04 D16
IN CHEN, A; CHEN, S; LUO, Y
PA (CHEN-I) CHEN A; (CHEN-I) CHEN S; (LUOY-I) LUO Y; (GENO-N) GENOSPECTRA INC
CYC 97
PI WO 2002016651 A2 20020228 (200232)* EN 60p <--

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2002055111 A1 20020509 (200235) <--
AU 2001086759 A 20020304 (200247) <--

ADT WO 2002016651 A2 WO 2001-US26561 20010824; US 2002055111 A1 Provisional US 2000-227896P 20000825, Provisional US 2001-292069P 20010517, US 2001-938798 20010824; AU 2001086759 A AU 2001-86759 20010824

FDT AU 2001086759 A Based on WO 200216651

PRAI US 2001-292069P 20010517; **US 2000-227896P 20000825**; US 2001-938798 20010824

AN 2002-280951 [32] WPIX

AB WO 200216651 A UPAB: 20020521

NOVELTY - Novel three-dimensional (3D) internal probe-carrier (PC) (IPC)/external PC (EPC), where IPC has a discrete through well having elongated bore structure traversing solid support (SS) from one surface to the other and defined by inner side wall, and where EPC has a discrete pillar having an elongated core and defined by exterior side wall on one surface of SS, is new.

DETAILED DESCRIPTION - Novel three-dimensional (3D) internal probe-carrier (PC) (IPC)/external PC (EPC), is new. IPC for binding a target molecule to a probe has SS having two surfaces, at least one discrete through well on SS which comprises an elongated bore structure traversing SS from the one surface to the other and defined by an inner side wall, where each well is individually identifiable by its position on SS, a light conducting region surrounding each well, and specific probe molecules attached to a discrete location on an inner side wall of the well. EPC has a support with a single surface, at lest one discrete pillar on the first surface of the solid support, the pillar comprising an elongated core and defined by at least one exterior side wall, where each pillar is individually identifiable by its position on the solid support, and at least one specific probe molecule attached to exterior side wall of the pillar.

INDEPENDENT CLAIMS are also included for the following:

(1) fabricating a three-dimensional IPC, comprising:

(a) providing a tube preform;

(b) creating an optical waveguide around the through well by providing a light guiding region around the through well bore;

(c) forming a stack of preforms by stacking several preforms in an orderly matrix of a honeycomb or chessboard pattern;

(d) fusing several preforms by heating the preform stack at or near a melting point of the preform material;

(e) extruding one or more preform stacks each that an outer diameter of the preform stack is reduced and an inner diameter of the individual preform is proportionally reduced in a first predetermined size;

(f) further extruding one end of the preform stack so that it is proportionally reduced to a second predetermined size;

(g) introducing probe containing fluid at an end of the preform stack reduced to the first predetermined size and distributing the probe fluid through the entire length of the preform stack; and

(h) cutting the preform stacks into chips or pins; and

(2) fabricating a three-dimensional EPC, comprising:

(a) providing an optical fiber comprising a core and an outer layer;

(b) affixing one or more probes to the outer surface of fiber so that the location of each probe is determinable;

(c) attaching one end of each of one or more fibers to a solid support;

(d) coating each probe-attached fiber with a removable, protective layer so that the fiber is held in place;

(e) attaching an end of each fibers to one another such that one end

of the fibers from a bundle while the other loose end is identifiable by an optical fiber; and

(f) establishing the identity of each fiber in the bundled end, and cutting the bundle into individual pillars and removing the protective layer, where the identity of each fiber in the pillar is established;

(3) 3D probe array (II) has a substrate formed of a substrate material, and has multiple probe wells (PWs) having a top and bottom surface, an inner side wall, an opening in the top and bottom surface, where a probe well (PW1) contains probes and light-conducting material (Ia) and a second material (Ib), where (Ia) and (Ib) are configured such that a light beam launched into the opening of PW1 in the top surface is transmitted by (Ia) and exits the opening of PW1 in the bottom surface;

(4) an array of pillars (III) comprising multiple pillars having proximal ends, distal ends, and side walls, which the proximal ends of the pillars are affixed to a surface of a substrate, and each of the pillars has a probe attached to the sidewalls of the pillars; and

(5) generating or manufacturing (M2) an array of capillaries.

USE - IPC and EPC are useful for binding a target molecule to a probe. IPC is useful for hybridizing a target molecule to a probe, by enabling a flow of hybridization fluid containing the target molecule across and through the elongated bore structure of IPC so that the target molecule is able to contact the probe, and reading a signal resulting from the hybridization. The method can also be performed by using EPC, where the method comprises contacting the probe attached to the exterior side wall of the pillar of EPC, with a hybridization fluid containing the target molecule and reading a hybridization signal resulting from the hybridization. (II)/(III) is useful for binding a target to probes in a probe array and for detecting target molecules bound to probe molecules in the array. M1 is useful for fabricating a three-dimensional IPC or EPC and M2 is useful for generating or manufacturing an array of capillaries. (All claimed).

ADVANTAGE - Novel 3D EPC and IPC increases the economy of reagents, compactness and readability of probe carriers. It is cost effective.
Dwg.0/13

TECH UPTX: 20020521

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Probe-carrier: In IPC, several different probes are attached to the inner side wall of SS at a density exceeding 100 preferably 500 different probes/square millimeter and EPC probes attached to the inner side wall of SS is preferably at a density exceeding 100 or 1000 different probes/square mm, where SS is from optical fiber, glass, silicon, polymer, plastic, ceramics and metal. The through well further comprising a light conduction region surrounding the elongated bore structure traversing SS, where the bore structure open at both the surfaces of SS, where one of the surface of SS is bonded to a second planar SS so that the bore structure is open at one surface and closed at the other surface. The probe is preferably form DNA, RNA, synthetic polynucleotides, oligonucleotides, antibodies, proteins, polypeptides, peptides, lectins, oligosaccharides,modified polysaccharides, synthetic composite macromolecules, functionalized nanostructures, synthetic polymers, modified or blocked nucleotides and nucleosides, modified or blocked amino acids, fluorophores, chromophores, ligands, chelates, haptens, drug compounds, cell receptors, lipids, cells, or combinations of these structures, or any other structures to which the target molecule or portions of the target molecule binds with specificity. IPC further comprises a chamber for a fluid containing the probe molecule which is preferably frozen by lyophilization, where the fluid is confined within the discrete well structure by capillary forces, and a protective film (polymer or metallic film) attached to at least one of surfaces of SS, where the surface of the film in contact with SS is hydrophobic. The inner wall surface of the bore structure is hydrophilic. In EPC, the pillars are in the form of short pins or rods arranged as a matrix on a planar SS so that the pattern and pitch of the matrix corresponds to a microtiter plate.

Preferred Array: In (II), (Ia) has a refractive index (RI1) and (Ib) has a refractive index (RI2) that is less than RI1 so that PW1 forms a light-conducting waveguide, and (Ia) preferably comprises a liquid in fluid contact with the inner side wall of PW1 and (Ib) comprises the side wall, or alternatively (Ia) comprises a first portion of PW1 that includes the inner side wall and (Ib) comprises a portion of the substrate or comprises a second portion of PW1 bound by first portion and an outer side wall of PW1, where (Ia) comprises silica doped with an impurity that increases RI of silica and a second portion comprises silica having a lower RI that the first portion. PWs comprises multiple capillaries bound together to form a bundle is an unordered or ordered bundle and the substrate comprises a binder that holds the capillaries together, where the binder comprises epoxy, silica, metal band, a plate having through-holes through which the capillaries pass, or a plate to which each of the bottom surfaces of PWs is attached. The opening in the top surface and bottom surface of PW1 form a portion of a channel through PW1, where the channel has a length and which channels has a cross-sectional area that is essentially constant or decreases along the length of the channel. (II) further comprises a base plate to which bottom surface of PW1 is attached and the probe wells are distributed across the substrate at a density greater than 400 probe wells/square cm, the probe comprise biological and chemical samples. In (III), the surface of the substrate is planar or is a rod having two ends and sidewall, where the surface of the substrate comprises the sidewalls, where the distal end of each pillar is free of biological and chemical sample and the longest axis of each pillar is less than 200 micro-m, and the pillars are distributed across the substrate at a density greater than 400 pillars/square cm of substrate surface, where each pillar have an electrically conductive core and are light-conducting pillars.
Preferred Method: M1 further comprises registering the proximal ends of capillaries to the distal ends preferably by launching light in to a distal end of a first capillary, observing the light exiting a proximal end of the first capillary and recording information that correlates the distal end of the first capillary to the proximal end of the first capillary, and the channel of each capillaries coated with a material so that the coating reflex light within the channel.

L49 ANSWER 16 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-268809 [31] WPIX
CR 2002-268868 [31]; 2002-403133 [43]
DNC C2002-079667
TI Multi-cell **substrate** useful in microarray applications comprises a microporous membrane, a non-porous **substrate** and a surface treatment.
DC A96 B04 D16
IN AMIN, M; MEYERING, M; OSTREICHER, E; ANDREOLI, R; CHESTERTON, R; MYERING, M
PA (CUNO-N) CUNO INC; (AMIN-I) AMIN M; (MEYE-I) MEYERING M; (OSTR-I) OSTREICHER E
CYC 23
PI WO 2002002585 A2 20020110 (200231)* EN 43p <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU BR JP
AU 2001071835 A 20020114 (200237) <--
US 2002086307 A1 20020704 (200247) <--
ADT WO 2002002585 A2 WO 2001-US21262 20010705; AU 2001071835 A AU 2001-71835 20010705; US 2002086307 A1 Provisional US 2000-216390P 20000706, US 2001-898102 20010703
FDT AU 2001071835 A Based on WO 200202585
PRAI **US 2000-224141P 20000810; US 2000-216229P 20000705 ; US 2000-216390P 20000706;** US 2001-898102 20010703
AN 2002-268809 [31] WPIX
CR 2002-268868 [31]; 2002-403133 [43]

AB WO 200202585 A UPAB: 20020725
NOVELTY - A multi-cell **substrate** comprises a substantially non-reflective microporous membrane formed by a phase inversion process and providing a fluorescence of about 300 - 700 nm, a non porous **substrate**, and a surface treatment operatively positioned between the microporous membrane and the non-porous **substrate** for covalently bonding the **substrate** to the membrane.

DETAILED DESCRIPTION - A multi-cell **substrate** comprises:

(a) a substantially non-reflective microporous membrane formed by a phase inversion process and providing a fluorescence of about 300 - 700 nm;

(b) a non porous **substrate**; and

(c) a surface treatment operatively positioned between the microporous membrane and the non-porous **substrate** for covalently bonding the **substrate** to the membrane.

The membrane comprises a phase-inversion support and several opaque solids that are substantially chemically non-reactive with the inversion support and intimately bound to, and/or partially/completely contained with the phase-inversion. The multi-cell **substrate** may also comprise an optically-passive **substrate** comprising the phase-inversion support and the opaque solids.

An INDEPENDENT CLAIM is also included for fabricating the multi-cell **substrate** involving:

(a) formulating a casting dope comprising a solvent, at least one non-solvent, opaque solids and polyamide(s);

(b) mixing and blending the casting dope to cause dissolution of the polyamide and opaque solids;

(c) producing an opaque solids-filled phase inversion casting dope;

(d) casting a thin portion of the opaque solids-filled phase inversion casting dope;

(e) quenching the casted portion of the opaque solids-filled phase inversion casting dope to form a **substrate**;

(f) applying the surface treatment to the **substrate**; and

(g) intermingling the **substrate** with the microporous membrane.

USE - For carrying a microarray of biological polymers and in microarray applications (both claimed), for micro-analytical diagnostic applications, in luminescent assays for detecting analytes in a sample and for simultaneous use of different fluorescently labeled tags for simultaneous detection of multiple analyte molecules.

ADVANTAGE - The **substrate** has a reflectance of not more than 50% of incident light at any wavelength within the range of wavelengths. The properties of the **substrate** are easily controlled. The **substrate** is more physically robust than the nitrocellulose membrane slides of the prior art and is relatively easily manufactured. The **substrate** minimizes or eliminates any glue/adhesive layer between the membrane and the solid **substrate** which adds thickness to the membrane/**substrate** combination. The surface treatment has no discernable finite thickness or mass which could add non uniformity to the overall thickness of the **substrate**. The surface treatment minimizes or eliminates its participation in the binding or detection of nucleic acid or protein analytes by the **substrate** and minimizes the interference of the substances used to connect the solid **substrate** portion to the porous membrane portion. The **substrate** has a regular surface on the micro scale and eliminates compatibility issues between the glue/adhesive and the analyte. The **substrate** is economically produced.
Dwg.0/6

TECH UPTX: 20020516
TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The surface treatment comprises a 3-aminopropyl triethoxysilane followed by treatment with a polyamido-polyamine epichlorohydrin resin. The **substrate** is Mylar, polypropylene, polycarbonate, polysulfone, polyamide or polyaramid

(preferably polyester or Mylar). The surface of Mylar is oxidized with sulfuric acid or corona discharge to enable it to bond to a polyamido polyamine epichlorohydrin polymer. The polyamide support is charge-modified. The phase inversion membrane is polysulfone, polyethersulfone or polyvinylidenedifluoride (PVDF). The phase inversion support is in the form of a membrane and charge-modified polyamides. The phase inversion support is hydrophilic and skinless.

TECHNOLOGY FOCUS - CERAMICS AND GLASS - Preferred Components: The **substrate** is glass or ceramic (preferably glass)

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The surface treatment is 3-aminopropyl triethoxysilane, N-(2-aminoethyl)-3-aminopropyl trimethoxysilane, 3-glycidoxypropyltrimethoxysilane, (10-carbomethoxydecyl) dimethylchlorosilane or 2-(3,4-epoxycyclohexyl)-ethyltrimethoxysilane. The **substrate** is acrylic. The phase inversion membrane is nylon 66, nylon 46 or nylon 6.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Components: The opaque solids are pigments or carbon particles having less than 5 microns in size. The carbon particles are substantially uniformly distributed throughout the polyamide support and may be partially or wholly incorporated into the polyamide support.

L49 ANSWER 17 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-263526 [31] WPIX
DNN N2002-204748 DNC C2002-078777
TI Detection of a target base sequence comprises using primer combined fine colloid particles.
DC B04 D16 **S03**
PA (NITE) NIPPON TELEGRAPH & TELEPHONE CORP
CYC 1
PI JP 2002034564 A 20020205 (200231)* 8p
ADT JP 2002034564 A JP 2000-219281 20000719
PRAI **JP 2000-219281 20000719**
AN 2002-263526 [31] WPIX
AB JP2002034564 A UPAB: 20020516
NOVELTY - Advancing primer-combined fine particles comprise an advancing primer containing an oligonucleotide chain complementary to the 3'-end portion of an antisense chain of a DNA having a target base sequence is combined to the surface of fine colloid particles.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for
(1) reversing primer-combined fine particles by combining a reversing primer containing an oligonucleotide chain complementary to the 3'-end portion of an antisense chain of a DNA having a target base sequence with the surface of fine colloid particles;
(2) a reagent for detecting a target base sequence containing the above advancing primer-combined fine particles and detecting the above reversing primer-combined fine particles; and
(3) a method for detecting a target base sequence by using the above reagent.
USE - The reagent is used for detecting a target base sequence.
Dwg.0/5

L49 ANSWER 18 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-257596 [30] WPIX
DNC C2002-076698
TI New biosensors with microchannels or sensing receptacles, useful for detecting biological molecules (e.g. polynucleotides), particularly for increasing sensitivity of optical assays while decreasing the required sample volume.
DC B04 D16
IN HO, C; WANG, T

PA (REGC) UNIV CALIFORNIA
CYC 96
PI WO 2002014462 A1 20020221 (200230)* EN 53p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001088249 A 20020225 (200245) <--
ADT WO 2002014462 A1 WO 2001-US25444 20010814; AU 2001088249 A AU 2001-88249 20010814
FDT AU 2001088249 A Based on WO 200214462
PRAI **US 2000-225077P 20000814**
AN 2002-257596 [30] WPIX
AB WO 200214462 A UPAB: 20020513

NOVELTY - Biosensors or chemical sensors, comprising a microchannel or a sensing receptacle, are new. The sidewall of the microchannel or sensing receptacle has been treated to reflect an optical signal so that the signal-to-noise ratio of the reflected optical or fluorescent signal is increased.

DETAILED DESCRIPTION - Biosensors or chemical sensors, comprising a microchannel or a sensing receptacle, are new. The sidewall of the microchannel or sensing receptacle has been treated to reflect an optical signal so that the signal-to-noise ratio of the reflected optical or fluorescent signal is increased. The sensing receptacle, in which a target molecule and a probe for the target molecule interact, is integrated with an electronic element consisting of a transistor, a diode and an integrated circuit. The sidewalls and bottom of the sensing receptacle have been treated to function as discrete electrodes capable of electrically concentrating a molecule in a predetermined region of the biosensor.

INDEPENDENT CLAIMS are also included for the following:

(1) a method of measuring a fluorescence signal comprising measuring the signal of a fluorescent molecule within the microchannel;

(2) a method of enhancing the optical measurement of a fluorescent signal of a fluorophore coupled to a molecule (e.g. polynucleotide or polypeptide) by measuring the fluorescent signal of the fluorophore coupled molecule within the microchannel; and

(3) a method for detecting a target molecule (i.e. polynucleotide or polypeptide) comprising:

(a) allowing the target molecule and a probe for the target molecule to interact within a first area on the biosensor comprising an ion sensitive filed effect transistor sensor and a separation channel;

(b) moving the target molecule and the probe for the target molecule that have interacted to a second area on the biosensor through the separation channel via electrophoresis; and

(c) sensing a signal generated by the interacted target molecule and the probe for the target molecule in the second area of the biosensor via the ion sensitive field effect transistor sensor.

USE - The biosensors are useful for detecting biological molecules, e.g. polynucleotides. The biosensors are particularly useful for increasing the sensitivity of optical assays while decreasing the sample volume required for detection.

Dwg.0/24

TECH UPTX: 20020513

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Biosensor: The sidewall of the microchannel has been treated so as to reflect an optical or fluorescent signal by coating the sidewall with a reflective film of aluminum, where the signal-to-noise ratio of the reflected optical or fluorescent signal is enhanced by at least 80 %. The microchannel has also been treated to reflect an optical or fluorescent signal by coating the sidewall with a reflective film of gold, where the signal-to-noise ratio

of the reflected optical or fluorescent signal is enhanced by at least 15 %. The microchannel has a cross-section geometrical shape consisting of a rhombus, a trapezoid, a v-groove or a rectangle. Preferably, the microchannel cross-section geometrical shape is a trapezoid. The microchannel is fabricated by KOH etching. The microchannel or receptacle is in a microchip comprising a material selected from silicon, glass or plastic. The sidewall of the microchannel is able or configured to aim or focus the reflected fluorescence signal in a desired direction. The cross-section geometrical shape of the sensing receptacle is configured to enhance the reflected signal-to-noise ratio. The sidewall of the sensing receptacle is constructed to aim or focus the reflected optical signal in a desired direction. The electronic element consists of an ion sensitive field effect transistor and a metal oxide semiconductor field effect transistor. The sensing receptacle is a microchannel, where two or more electrodes are integrated into the microchannel. The dielectric strength of the microchannel is enhanced by including a dielectric material within the channel, particularly SiO_2. The electronic element is a metal oxide semiconductor field effect transistor comprising a source and a drain fabricated so that the source and drain of the metal oxide semiconductor field effect transistor are on the sidewalls of the microchannel. The separation is also a microchannel. The electrodes are made by coating and patterning the receptacle with aluminum (where the electrodes increase the biosensor's sensitivity for detecting a molecule by at least 500 %) or gold.

Preferred Method: The method further comprises selecting a cross-section geometrical shape for the microchannel that enhances the reflected signal-to-noise ratio. The fluorescence signal is measured by a laser induced fluorescence system. The fluorescence molecule comprises a polynucleotide coupled to a fluorescein moiety. The fluorophore coupled molecule is a polynucleotide. In particular, the fluorophore coupled polynucleotide comprises a molecular beacon probe having a 5' end labeled with a fluorescein moiety and a 3' end labeled with a fluorescein quenching moiety. The volume of the media having the fluorophore coupled molecule is less than 50 picoliters. The molecular beacon probe is used to detect DNA, where the concentration of DNA detected is less than 0.1 zmol.

L49 ANSWER 19 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-257382 [30] WPIX
DNN N2002-199266 DNC C2002-076581
TI Support disk in the form of a CD for use in hybridization assays, has microfluidic components, machine-readable data and a recess into which a microarray chip can be inserted for receiving an array of biological or chemical samples.
DC B04 D16 **J04 S03**
IN KUENNECKE, W
PA (TRAC-N) TRACE BIOTECH AG
CYC 96
PI WO 2002010448 A2 20020207 (200230)* DE 33p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
DE 10037687 A1 20020214 (200230) <--
AU 2001083975 A 20020213 (200238) <--
ADT WO 2002010448 A2 WO 2001-EP8917 20010801; DE 10037687 A1 DE 2000-10037687 20000801; AU 2001083975 A AU 2001-83975 20010801
FDT AU 2001083975 A Based on WO 200210448
PRAI **DE 2000-10037687 20000801**
AN 2002-257382 [30] WPIX
AB WO 200210448 A UPAB: 20020513
NOVELTY - A support disk in the form of a conventional CD for assays,

comprising an adapter with a recess for receiving an array of biological or chemical samples, a microfluidic component with a pattern of channels for liquid and/or machine-readable identifying, control and calculation data, is new.

DETAILED DESCRIPTION - A support disk for assays is in the form of a conventional CD and has:

(a) an adapter comprising a recess into which a functional component comprising a microarray chip, glass microscope slide, paper support or plastic sheet can be inserted for receiving an array of biological or chemical samples;

(b) a microfluidic component with a pattern of channels for liquid; and/or

(c) machine-readable identifying, control and calculation data.

INDEPENDENT CLAIMS are also included for the following:

(1) the adapter;

(2) applying an array of biological or chemical materials to the disk;

(3) forming an oligonucleotide array comprising:

(a) preparing a support disk (10) with an analysis site (11), on which photochemically activatable coupling materials are arranged on coupling sites (20') and a light source (30) for activating the coupling materials on a single coupling site;

(b) coupling the coupling material at a single site with an oligonucleotide or oligonucleotide component by applying it and illuminating it; and

(c) rotating the disk and/or shifting the light source radially, so that another site is illuminated;

(4) apparatus for carrying out the coupling method;

(5) a method for carrying out a hybridization assay comprising preparing an oligonucleotide array by the method describe above and applying a nucleic acid to the coupling sites; and

(6) a CD reader for use in processing the data from the hybridization assay.

USE - The disk is useful for carrying out hybridization assays (claimed).

Dwg.0/4

L49 ANSWER 20 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-255553 [30] WPIX
DNN N2002-197606 DNC C2002-076172
TI Screening modulator of desired gene by culturing various promoter probe-reporter gene in semi-solid media in a multi-well plate, and subjecting the living cells to a battery of test compounds of varying concentrations.
DC B04 D16 **S03** T01
IN ALBANO, C R; BENTLEY, W E; RAO, G
PA (ALBA-I) ALBANO C R; (BENT-I) BENTLEY W E; (RAOG-I) RAO G
CYC 1
PI US 2002015940 A1 20020207 (200230)* 14p <--
ADT US 2002015940 A1 Provisional US 2000-193036P 20000329, US 2001-813315 20010321
PRAI **US 2000-193036P 20000329**; US 2001-813315 20010321
AN 2002-255553 [30] WPIX
AB US2002015940 A UPAB: 20020513

NOVELTY - Screening (M1) a compound that effects expression of a desired gene by culturing various promoter probe-reporter gene (green fluorescent protein (GFP)) in semi-solid media in a multi-well plate, where the promoters are systemically cloned upstream of a readily measurable reporter gene, and subjecting or exposing the living cells to a battery of test compounds of varying concentrations, is new.

DETAILED DESCRIPTION - Screening (M1) a compound that effects expression of a desired gene, comprising:

(a) preparing an array of transformed cell cultures (I) each forming

a loci in the array, where each (I) in the array comprises:
(i) a series (S1) of DNA molecules, with each comprising a DNA sequence of a promoter of a different desired gene (G1) encoding a reporter molecule (RM), so that expression of RM is controlled by the promoter, and
(ii) a series (S2) of DNA molecules with each comprising a DNA sequence encoding G1, so that expression of a product of G1 is controlled by the promoter;
(b) exposing the transformed cell cultures in the array to a test compound;
(c) at each loci, assaying for a reporter characteristic of the reporter molecule; and
(d) identifying loci in the array which show a difference in the reporter characteristic relative to a control, and identifying the gene present at loci to thereby identify a test compound which effects expression of the gene, where cells constituting the culture are not lysed during the method.
An INDEPENDENT CLAIM is also included for a system (II) for (M1) comprising:
(a) a computer with a central processing unit (CPU) and a memory;
(b) a membrane comprising an array of cell cultures where the cell cultures comprises immobilized cells or is (I);
(c) a source of light adapted to emit light onto a selected cell culture from the array of cell cultures;
(d) a photodiode adapted to scan a characteristic generated by RM; and
(e) an interface adapted to receive signals from the photodiode and provide information to the computer, where the computer is adapted to receive the information and perform the screening.
ACTIVITY - Cytostatic.
MECHANISM OF ACTION - E. coli oxidative stress response system modulator (claimed).
No biological data is given.
USE - M1 is useful for screening a compound that effects (modulates) expression of a desired gene, which is especially a gene whose increased or reduced expression is associated with cancer, and the test compound thus identified is an anti-cancer compound (claimed).
ADVANTAGE - The method is adaptable to a high throughput-screening program for elucidating specific gene expression under a variety of conditions. The labor is shifted upstream of the experiment, i.e. to the creation of the clones. Moreover, the experiments themselves become trivial by comparison, and are almost free of artifacts to which gene-chip experiments are subject.
Dwg.0/7

TECH UPTX: 20020513
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In M1, the difference in reporter characteristic relative to a control is preferably a reduction/increase of the reporter characteristic relative to the control, where the test compound which inhibits/enhances expression of G1 is identified. (I) is preferably bacterial cell cultures, and RM is green fluorescent protein (GFP), and G1 is a member of the Escherichia coli oxidative response system, which is selected from gyrA, katG, micF, osm Y, uspA, katF, recA, zwf, dnaK, clpB, umuDC, merR, ada, dinD, soi28, sodA and nfo. The cells of (I) are preferably cultured in the array and the assaying step is carried over the course of time or at an end point so as to examine the effect of the resulting identified test compound on the rate of expression of G1, and the DNA molecules of S2 is heterologous or native to the cell cultures.

L49 ANSWER 21 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-225941 [28] WPIX
CR 2002-328525 [17]; 2002-339267 [17]
DNN N2002-173337 DNC C2002-068793

TI Thermal gradient apparatus, useful for analysis of biological macromolecules, comprises semiconducting wafer, two adjacent electrical connectors and power source.
DC B04 D16 T01 U11
IN BLUMENFELD, M; CIBUZAR, G T; FISHER, M; VAN NESS, B G; WILLIAMSON, F
PA (BLUM-I) BLUMENFELD M; (CIBU-I) CIBUZAR G T; (FISH-I) FISHER M; (VNES-I) VAN NESS B G; (WILL-I) WILLIAMSON F
CYC 1
PI US 2002015995 A1 20020207 (200228)* 45p <--
ADT US 2002015995 A1 Div ex US 2000-630172 20000801, US 2001-853806 20010511
PRAI **US 2000-630172 20000801**; US 2001-853806 20010511
AN 2002-225941 [28] WPIX
CR 2002-328525 [17]; 2002-339267 [17]
AB US2002015995 A UPAB: 20020613

NOVELTY - A thermal gradient apparatus comprising a semiconducting wafer, two adjacent electrical connectors on the wafer, and a power source, where each of the connectors is attached to the wafer at an attachment site, a gap is disposed between the two attachment sites and the power source is connected to the wafer through the electrical connectors, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) generating a temperature gradient;

(2) analyzing (M1) biological macromolecules comprising establishing a temperature gradient using the thermal gradient apparatus and evaluating the samples to determine thermal stability of complexes formed with the biological macromolecules in the samples, where the samples are evaluated by measuring a property of the sample;

(3) conducting nucleic acid hybridization comprising establishing a temperature gradient using the thermal gradient apparatus and performing a hybridization protocol on the sample to determine temperature effect based on the gradient; and

(4) assessing binding complex interactions comprising establishing a temperature gradient using the thermal gradient apparatus and evaluating the samples to determine thermal stability of the binding complex on the stratum.

USE - For use in generating temperature gradient useful for the analysis of molecules, preferably biological macromolecules.

ADVANTAGE - The inventive apparatus is able to generate stable temperature gradient.

DESCRIPTION OF DRAWING(S) - The figure is a schematic diagram of the thermal gradient apparatus.

Semiconducting wafer 110
Electrical connectors 114a, 114b
Electrical wires 116a, 116b
Electrical transformer 120
Power source 126
Temperature sensor 130
Gap 134
Temperature controller 136
Relay switch 140
Dwg.1/11

TECH UPTX: 20020502

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Components: The semiconducting wafer is of rectangular shape, and has clipped corners. Both attachment sites are located near the rectangular edges. The two attachment sites are spaced at a distance of 2-180 mm. A temperature gradient formed on the wafer is perpendicular to an attachment line derived from connecting the two attachment sites. The electric connectors and the power source are connected by electrical wires (116a, 116b). The thermal gradient apparatus further comprises control circuitry provided between the wafer and the power source. The control circuitry comprises a temperature sensor (130) disposed in the gap and connected to a temperature controller (136), and an electrical transformer (120)

connected in series between the power source and the electrical connectors. A feedback control is provided between the temperature sensor and the temperature controller to maintain the measurement of the temperature sensor within a selected range. The feedback control opens or closes a relay switch (140). Stratum are disposed in wafer, and consist of DNA chip, protein chip, fluidic cell, microscopic slide, liquid, coverslip, and/or acrylamide gel. The stratum are provided with samples of molecules, labeled probes, or members of a binding complex. The stratum are made of glass, silicon, or plastic.
Preferred Method: The temperature gradient is generated by thermoelectric Peltier device, and formed at 0.1-1 (preferably 0.25-0.7) degrees C/mm.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Components: The semiconducting wafer is a silicon wafer comprising a doping agent consisting of boron, phosphorus, or arsenic.
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Components: The samples of molecules consist of nucleic acid molecules, polypeptides, carbohydrates, lipids, hormones, and/or drugs. The labeled probes are fluorescent labeled probes, chemiluminescent labeled probes, or radiolabeled probes. The polypeptides consist of antigens, antibodies, enzymes, receptors, or its fragments. The binding complex comprises nucleic acid duplex, polypeptides, nucleic acid:polypeptide complex, nucleic acid:drug complex, antigen:antibody complex, receptor:drug complex, lipid:polypeptide complex, or carbohydrate:polypeptide complex. The biological macromolecules are nucleic acids, antigens, antibodies, enzymes, receptors and their fragments. The stratum comprises a DNA chip with the nucleic acids, especially an acrylamide gel having the nucleic acids. Evaluating comprises characterizing the thermal stability of a complex formed by 2 singled stranded nucleic acid molecules having base mismatches. It comprises adding a labeled probe, washing away unbound probe and detecting the activity of the labeled probe at various positions on the DNA chip. Activity of the labeled probe is correlated with temperature of the sample at various positions on the DNA chip. Alternatively evaluating comprises characterizing the thermal stabilities of nucleic acid hybrids formed with primers for use in polymerase chain reaction protocols. The temperature gradient is between 20-45 degrees C.

L49 ANSWER 22 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-225858 [28] WPIX
CR 2001-548994 [47]
DNC C2002-068751
TI Apparatus for conducting chemical/biochemical reaction on solid surface within enclosed chamber, comprises substrate and cover which form reaction chamber which facilitates mixing of components and reduces unwanted reactions.
DC A89 B04 D16
IN HOTZ, C Z; OVERMAN, L B; SCHEMBRI, C T
PA (HOTZ-I) HOTZ C Z; (OVER-I) OVERMAN L B; (SCHE-I) SCHEMBRI C T
CYC 1
PI US 2002001839 A1 20020103 (200228)* 19p <--
ADT US 2002001839 A1 Div ex US 1999-343372 19990630, US 2001-900294 20010706
PRAI **US 1999-343372 19990630**; US 2001-900294 20010706
AN 2002-225858 [28] WPIX
CR 2001-548994 [47]
AB US2002001839 A UPAB: 20020502
NOVELTY - An apparatus (I) for use in conducting a (bio)chemical reaction on a solid surface within an enclosed chamber, is new.
DETAILED DESCRIPTION - An apparatus (I) for use in conducting a (bio)chemical reaction on a solid surface within an enclosed chamber comprising:
(a) a substrate having a substantially planar surface with a portion of the surface representing a reaction area on which chemical or biochemical reactions are conducted;

(b) a plastic cover having a peripheral lip which sealingly contacts the substrate surface about the reaction area, where the cover and the reaction area form an enclosure having an interior space comprising a reaction chamber;

(c) a fastening unit for immobilizing the cover on the substrate surface and providing a temporary, watertight seal between the cover and the reaction area; and

(d) an unit for introducing the fluid into the reaction chamber, is new.

INDEPENDENT CLAIMS are also included for the following:

(1) a device (II) for conducting hybridization assay within an enclosed hybridization chamber, comprising:

(a) a substrate having a surface with a portion of surface representing a hybridization region;

(b) several oligonucleotide probes bound to the substrate surface within the hybridization region and arranged in a spatially defined and physically addressable manner;

(c) a cover which sealingly contacts the substrate surface about the hybridization region, and forms an enclosure having an interior space comprising a hybridization chamber;

(d) contained within the hybridization chamber, a sample fluid comprising a target molecule which may hybridize to a surface-bound molecular probe within the hybridization region; and

(e) the sample fluid additionally comprises a surfactant present at a concentration effective to reduce nonspecific binding and promote mixing of components within the sample fluid;

(2) mixing (III) a fluid in an enclosed chamber having a height less than approx. 0.5 mm, by providing a chamber having a height of less than 0.5 mm, introducing into the chamber, a fluid containing molecular components and an air bubble, sealing the chamber and moving the chamber so as to create movement of the bubble within the fluid, where mixing of the molecular components within the fluid is effected by displacement of the fluid as the bubble moves within the chamber; and

(3) a kit for carrying out hybridization in an enclosed hybridization chamber, comprising a substrate, probes and cover as in (II), and a surfactant effective to promote mixing and substantially reduce nonspecific binding in a hybridization assay conducted within the chamber.

USE - (I) is useful for conducting a chemical or biochemical reaction on a solid surface within an enclosed chamber. (II) is useful for conducting a hybridization assay within an enclosed hybridization chamber. The method comprises introducing sample fluid comprising a target molecule which may hybridize to a surface-bound molecular probe within the hybridization region, a hybridization buffer, and a surfactant at a concentration effective to substantially reduce nonspecific binding and promote mixing of components within the sample fluid and maintaining hybridization conditions within the chamber for a period of time sufficient to allow hybridization between the target molecule and a surface-bound molecular probe to occur. (III) is useful for mixing a thin film of fluid in an enclosed chamber (claimed). (I) and (II) are useful in conducting hybridization reactions of biopolymers such as DNA, RNA, oligonucleotides, peptides, polypeptides, proteins, and antibodies.

ADVANTAGE - In (I), mixing of components within the chamber is facilitated and occurrence of unwanted reactions is substantially reduced. The reaction chamber prevents the drying out of its contents even at elevated temperatures, and can be readily assembled and taken apart. In (II), background signals are significantly reduced with the functionalized substrate surface and with hybridization solutions comprising surfactants.

DESCRIPTION OF DRAWING(S) - The figure shows the exploded view of apparatus used for conducting a chemical or biochemical reaction on a solid surface within an enclosed chamber.

Substrate 2
Plastic cover 3
Dwg.1/9

TECH UPTX: 20020502
TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Arrangement: The reaction area is bound to or adapted to bind to molecular moieties which comprise molecular probes. (I) further comprises several molecular probes bound to the substrate surface within the reaction area and arranged in a spatially defined and physically addressable manner. The molecular probes are oligonucleotide or polypeptide probes, or comprised of cDNA or polymerase chain reaction (PCR) products. The cover is comprised of a material that is chemically or physically stable under conditions employed in hybridization assays, and is thermally stable at 50 degrees C. The cover is comprised of polypropylene, polyethylene or acrylonitrile-butadiene-styrene that is chemically inert or non-stick. The substrate is comprised of glass, plastic, silicon or fused silica. The dimensions of the cover, the peripheral lip, and the reaction area are such that the reaction chamber has a volume of 0.2-312 micro liter. The reaction chamber has a volume of 1-200 micro liter, and the reaction area is 4-500 mm2, preferably 20-350 mm2. The unit for introducing fluid into the reaction chamber comprises at least one port in the cover. In (II), the substrate surface is functionalized with a mixture of a first silane providing surface -Si-R1 groups and a second silane providing surface -Si-(L)n-R2 groups, where:
R1 = a chemically inert moiety;
L = a linking group;
n = 0 or 1; and
R2 = a functional group enabling binding of the oligonucleotide probes.
(II) further comprises a fastening unit and an unit for introducing sample fluid into hybridization chamber. An air bubble is present within the hybridization chamber. The sample fluid further comprises a hybridization buffer. The surfactant is anionic (e.g. sodium, potassium, ammonium or lithium salt of lauryl sulfate), cationic, amphoteric, nonionic surfactants (polymeric or polyethylene oxide), or their combinations. The surfactant represents 0.1-10 weight %, preferably 0.5-5 or 0.75-5 weight % of the sample fluid, and comprises a combination of polyethylene oxide and lithium lauryl sulfate. The polypeptide oxide represents up to 1 weight % of the sample fluid, and the lithium lauryl sulfate represents up to 0.5 weight % of the sample fluid.

L49 ANSWER 23 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-218861 [28] WPIX
DNN N2002-167881 DNC C2002-067090
TI Biochemical analysis unit consists of **substrate** made of material capable of attenuating radiation and/or light energy and formed with number of holes, and number of absorptive regions formed in every hole.
DC B04 D16 **J04 S03**
IN OGURA, N
PA (FUJF) FUJI PHOTO FILM CO LTD
CYC 27
PI EP 1178314 A2 20020206 (200228)* EN 70p <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2002016009 A1 20020207 (200228) <--
US 2002061534 A1 20020523 (200239) <--
ADT EP 1178314 A2 EP 2001-118133 20010726; US 2002016009 A1 US 2001-918500 20010801; US 2002061534 A1 Div ex US 2001-918500 20010801, US 2001-21050 20011219
PRAI JP 2001-199183 20010629; **JP 2000-234776 20000802**; JP 2001-100942 20010330
AN 2002-218861 [28] WPIX
AB EP 1178314 A UPAB: 20020502
NOVELTY - A biochemical analysis unit (I) (1), comprising a **substrate** made of a material capable of attenuating radiation energy and/or light energy and formed with a number of holes (3), and a number of absorptive regions (4) formed by forming an absorptive region in

every hole, is new.

USE - (I) is useful in a biochemical analyzing method which comprises preparing a biochemical analysis unit by spotting specific binding substances, which can specifically bind with a substance derived from a living organism and whose sequence, base length, composition, etc., are known, in a number of absorptive regions, each of which is formed in a number of holes formed in a **substrate** made of a material capable of attenuating radiation energy and specifically binding a substance derived from a living organism and labeled with a radioactive labeling substance with the specific binding substances, superposing the biochemical analysis unit on a stimulable phosphor sheet in which a stimulable phosphor layer is formed so that the stimulable phosphor layer faces the number of absorptive regions, thus exposing the stimulable phosphor layer to the radioactive labeling substance contained in the number of absorptive regions, irradiating the stimulable phosphor layer exposed to the radioactive labeling substance with a stimulating ray, thus exciting stimulable phosphor contained in the stimulable phosphor layer, photoelectrically detecting stimulated emission released from the stimulable phosphor contained in the stimulable phosphor layer, thus producing biochemical analysis data, and effective biochemical analysis based on the biochemical analysis data (claimed).

ADVANTAGE - In (I), even in the case where the absorptive regions are formed at a high density, when a stimulable phosphor layer formed on a stimulable phosphor sheet is exposed to a radioactive labeling substance contained in the number of absorptive regions, electron beams (beta rays) released from the radioactive labeling substance contained in the individual absorptive regions are reliably prevented from being scattered in the **substrate** and advancing to regions of the stimulable phosphor layer that should be exposed to electron beams released from absorptive regions formed in neighboring holes. Therefore, it is possible to efficiently prevent noise caused by the scattering of electron beams released from the radioactive labeling substance from being generated in biochemical analysis data produced by irradiating the stimulable phosphor layer exposed to the radioactive labeling substance with a stimulating ray and photoelectrically detecting stimulated emission released from the stimulable phosphor layer and to produce biochemical analysis data having a high quantitative accuracy.

DESCRIPTION OF DRAWING(S) - The drawing shows a schematic perspective view showing one example of a scanner for reading data of a radioactive labeling substance recorded in a number of the dot-like stimulable phosphor layer regions formed on the stimulable phosphor sheet and fluorescence data recorded in the absorptive regions formed in a number of through-holes of the biochemical analysis unit and producing biochemical analysis data.

Biochemical analysis unit 1

Hole 3

Absorptive region 4.

Dwg.6/25

TECH UPTX: 20020502

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Unit: In (I), the absorptive regions are selectively labeled with at least one kind of a labeling substance selected from a radioactive labeling substance, a labeling substance which generates chemiluminescent emission when it contacts a chemiluminescent **substrate** and a fluorescent substance by spotting specific binding substances whose sequence, base length, composition, etc. are known, and specifically binds or hybridizes with a substance derived from a living organism and is labeled with at least one kind of the labeling substance with the specific binding substances. The substance derived from a living organism is specifically bound with specific binding substances by a reaction selected from hybridization, antigen-antibody reaction and receptor-ligand reaction. The number of absorptive regions are formed by charging an absorptive material in the number of holes formed in the **substrate**. Each of the

number of holes is formed as a through hole or recess. The **substrate** is formed of a flexible material. (I) comprises an absorptive **substrate** formed of an absorptive material and a perforated plate formed with a number of through holes and made of a material capable of attenuating radiation energy and light energy, where the perforated plate is closely contacted with at least one surface of the absorptive **substrate** to form a number of absorptive regions of the absorptive **substrate** in the number of through-holes formed in the perforated plate. The perforated plate is in close contact with both surfaces of the absorptive **substrate**. The perforated plate or **substrate** is formed with a gripping portion by which the perforated plate can be gripped. (I) is formed with 10 or more holes, preferably 10000 or more holes. Each of the number of holes has a size of less than 5, preferably less than 0.1 square mm. The number of holes are formed at a density of 10 or more/square cm, preferably 10000 or more/square cm. The material capable of attenuating radiation energy and/or light energy has a property of reducing the energy of radiation and/or light to 1/5 or less, preferably 1/100 or less when the radiation and/or light travels in the material by a distance equal to that between neighboring absorptive regions. The **substrate** or perforated plate is formed of a material selected from metal, ceramic and plastic material. The absorptive material comprises a porous material (which comprises a carbon material or a material capable of forming a membrane filter) or a fiber material.

L49 ANSWER 24 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-217233 [27] WPIX
DNN N2002-166432 DNC C2002-066524
TI Protein microarray for screening complex chemical or biological samples to identify, isolate, and/or quantify components within complex samples, includes solid support, linker and protein or protein fragment.
DC B04 D16 **S03**
IN CARDONE, M H; MACBEATH, G; MARKS, J D; NIELSEN, U; SINSKY, A; SORGER, P
PA (MASI) MASSACHUSETTS INST TECHNOLOGY; (CARD-I) CARDONE M H; (MACB-I) MACBEATH G; (MARK-I) MARKS J D; (NIEL-I) NIELSEN U; (SINS-I) SINSKY A; (SORG-I) SORGER P
CYC 96
PI WO 2002012893 A2 20020214 (200227)* EN 49p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001077245 A 20020218 (200244) <--
US 2002076727 A1 20020620 (200244)
ADT WO 2002012893 A2 WO 2001-US24264 20010803; AU 2001077245 A AU 2001-77245 20010803; US 2002076727 A1 Provisional US 2000-222763P 20000803, US 2001-921655 20010803
FDT AU 2001077245 A Based on WO 200212893
PRAI **US 2000-222763P 20000803**; US 2001-921655 20010803
AN 2002-217233 [27] WPIX
AB WO 200212893 A UPAB: 20020429
NOVELTY - A protein microarray (I) comprising a solid support (10), a linker (20) and a protein or protein fragment, is new. The linker is covalently attached to the solid support, and the protein or protein fragment has a terminus that is capable of forming a covalent bond with the linker.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) attachment of a protein to a support surface, comprising:

(a) covalently attaching a bovine serum albumin (BSA) to a solid support surface;

(b) forming an activated carbamate group or activated ester group on the exposed surface of the molecule; and

(c) exposing the activated carbamate or ester group to a binding element comprising an amine to form a covalent bond between the carbamate or ester group of the molecule and the amine group of the binding element.

(2) attachment of protein to a support surface (M2), comprising:

(a) providing a support surface comprising a first chemical group available for reaction;

(b) providing a capture protein comprising a first terminus and a second terminus, where the first terminus is capable of binding to the ligand and the second terminus comprises a second chemical group; and

(c) forming a covalent bond between the first and second chemical groups, thus attaching the capture protein to the support surface at the second terminus of the capture protein;

(3) identification of small molecule that regulates protein binding (M3) comprising:

(a) attaching a capture protein (30) on support surface, exposing the **substrate** surface to a ligand for the capture protein and small molecule(s);

(b) and detecting the presence or absence of binding between the capture protein and the ligand;

(4) identification of a small molecule that selectively affects a cellular pathway (M4), comprising:

(a) attaching a microarray of capture proteins on a support surface comprising proteins that act in a cellular pathway;

(b) exposing the **substrate** surface to at least one ligand of the capture proteins and at least one small molecule;

(c) detecting a change in binding, which results from interaction with the small molecule, between the capture proteins and ligand;

(5) labeling an antigen (M5) comprising digesting the antigen with a protease to produce multiple peptides, so that at least one of the peptides is capable of receiving a label at a region of the peptide that does not interfere with binding between an epitope on the peptide and an antibody or antibody fragment;

(6) detection of phosphorylated protein (M6) comprising:

(a) fragmenting a candidate protein into peptides comprising target peptide with phosphorylation site;

(b) exposing the peptides to an antibody or antibody fragment having affinity for an epitope on the target peptide;

(c) selecting the target peptide based on affinity of the target peptide for antibody or antibody fragment; and

(d) conducting mass spectrometry on the target peptide; and

(7) studying a cellular event (M7) comprising:

(a) attaching a capture molecule on a support surface;

(b) exposing the **substrate** surface to a solution containing cellular organelle; and

(c) capturing the organelle through binding between the capture molecule and the ligand.

USE - The microarray is useful for screening complex chemical or biological samples to identify, isolate and/or quantify components within a sample based on their ability to bind to specific or wide variety of binding elements.

ADVANTAGE - The inventive microarray enables high-throughput screening of very large numbers of compounds. It paves the way for extensive and efficient screening using antibodies and similar molecules.

DESCRIPTION OF DRAWING(S) - The figure shows proximal phospho-affinity mapping.

Solid support 10

Linker 20

Capture protein 30

Dwg.2/11

TECH UPTX: 20020429

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The forming step of

(M1) comprises exposing BSA to a reagent to form a N-hydroxy succinimide group. The binding element is a protein, preferably s single chain antibody or fragment. The method further comprises blocking any activated carbamate or ester groups that have not bound to the binding element.
The capture protein of (M2) comprises a terminal cysteine, the terminal cysteine is at the carboxy end. The forming step comprises chemically reducing the cysteine.
(M3) and (M4) comprise attaching the capture protein to a BSA-NHS slide. The support surface is functionalized with aldehyde groups. The microarray comprises at least 1,000 spots per cm2. (M3) further comprises fusing the capture protein to a GST protein. Both methods also comprise detecting the binding between the capture protein and ligand using fluorescent dye, which comprises a hydrophilic polymer group, preferably polyethyleneglycol. Detection of binding may also be through a phage labeled with an antibody fragment. The contact protein and ligand comprise a related family of proteins, the ligand preferably comprises the Bcl-2 family of proteins.(M4) further comprises using mass spectrometry to quantify the change.
(M5) further comprises using a succinimidyl ester dye, preferably Cy3, Cy5 or an Alexa dye, to label the peptide. Only a terminal primary amine of the peptide is labelled where the epitope is internal. The antigen is digested with trypsin.
The candidate protein of (M6) is digested with a protease, preferably trypsin. An scFV is panned against the epitope. The antibody is immobilized onto a solid support. The detection step comprises detecting a change in the molecular weight of a subset of the target peptide using Matrix-Associated Laser Desorption Ionization (MALDI) mass spectrometry. The method also comprises immunizing a monoclonal or polyclonal antibody against the epitope. The epitope is less than 15, preferably less than 10 amino acids, away from the phosphorylation site and is less than 10, preferably less than 5, amino acids.
The capture molecule of (M7) comprises an antibody or fragment. The method further comprises studying a protein associated with the captured organelle, which is preferably a mitochondria. The ligand is a voltage dependent anion channel receptor uniquely associated with the mitochondrial membrane. The solution is a whole cell extract or its fraction. Detection comprises using fluorescent dye, which comprises a hydrophilic polymer group, preferably polyethyleneglycol or through a phage labeled with an antibody fragment. The dye has a potentiometric quality for recognizing an intact voltage gradient of the organelle.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The terminus is carboxy terminus. The linker is maleimide, vinyl sulfone, or N-hydroxy succinimide group. The protein or protein fragment is an antibody or antibody fragment (preferably single-chain antibody). Preferred Properties: The microarray has at least 1000 (preferably at least 2000) spots/cm2.

TECHNOLOGY FOCUS - CERAMICS AND GLASS - Preferred Component: The solid support is glass.

L49 ANSWER 25 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-206357 [26] WPIX
DNN N2002-157148 DNC C2002-063286
TI Manipulating moieties such as cells, cellular organelles, viruses, or molecules, in a microfluidic application, involves coupling it to the surface of a binding partner to form a complex.
DC B04 D16 **S03**
IN CHENG, J; WANG, X; WU, L; XU, J; YANG, W
PA (UYQI) UNIV QINGHUA; (AVIV-N) AVIVA BIOSCIENCES CORP
CYC 93
PI WO 2002012896 A1 20020214 (200226)* EN 109p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
CN 1337580 A 20020227 (200234) <--
AU 2000074922 A 20020218 (200244) <--

ADT WO 2002012896 A1 WO 2000-US25381 20000915; CN 1337580 A CN 2000-122631 20000808; AU 2000074922 A AU 2000-74922 20000915

FDT AU 2000074922 A Based on WO 200212896

PRAI **US 2000-636104 20000810; CN 2000-122631 20000808**

AN 2002-206357 [26] WPIX

AB WO 200212896 A UPAB: 20020424

NOVELTY - Manipulating a moiety in a microfluidic application, comprising coupling it onto-the surface of a binding partner to form a complex, and manipulating the complex with a physical force in a chip format, is new. The manipulation uses combination of an external structure, and a structure that is built into the chip.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) isolating an intracellular moiety from a target cell, comprising:

(a) coupling a target cell to be isolated from a biosammple onto a surface of a binding partner of the target cell to form a complex;

(b) isolating the complex with a physical force in a chip format;

(c) obtaining an intracellular moiety from the target cell;

(d) coupling the obtained intracellular moiety onto the surface of a second binding partner of the intracellular moiety to form a complex; and

(e) isolating the complex with a physical force in a chip format;

(2) generating a cDNA library in a microfluidic application, comprising:

(a) coupling a target cell to be isolated onto a surface of a binding partner;

(b) isolating the target cell-binding partner complex with a physical force in a chip format;

(c) lysing the target cell;

(d) decoupling and removing the binding partner from the lysed target cell;

(e) coupling mRNA to be isolated from the lysed target cell onto the surface of a second binding partner of the mRNA;

(f) isolating the mRNA-binding partner complex with a physical force in a chip format; and

(g) transporting the isolated complex to a different chamber and reverse transcribing the transported mRNA into a cDNA library;

(3) determining gene expression in a target cell in a microfluidic application, comprising:

(a) steps (a)-(f) of (2); and

(b) determining the quantities of the isolated mRNA molecules; and

(4) kit for manipulating a moiety in a microfluidic application, comprising:

(a) a binding partner onto which a moiety can be bound;

(b) means for coupling the moiety onto the surface of the binding partner; and

(c) a chip on which the complex can be manipulated with a physical force.

USE - For manipulating cells, organelles, virus, or molecules, for generating a cDNA library, for determining gene expression in a target cell, and for isolating an intracellular moiety from target cells, such as blood cells (claimed).

Dwg.0/15

TECH UPTX: 20020424

TECHNOLOGY FOCUS - BIOLOGY - Preferred Method: The moiety is a cell, cellular organelle, virus, molecule, or aggregate. The cell is an animal, plant, fungus, bacterium, or recombinant cell. The organelle is a nuclei,

mitochondrion, chloroplast, ribosome, endoplasmic reticulum, Golgi apparatus, lysosome, proteasome, secretory vesicle, vacuole, or microsome. The molecule is an amino acid, peptide, protein, nucleoside, nucleotide, oligonucleotide, a nucleic acid, vitamin, monosaccharide, oligosaccharide, carbohydrate, or lipid. The binding partner is a cell, cellular organelle, virus, microparticle, or aggregate. The microparticle is 0.01 to several thousand micro-m. Where the moiety is DNA, the binding partner is a porous bead and the DNA is reversibly absorbed onto the surface of the porous bead in a buffer containing high salt concentration. The DNA binds to the binding partner by sequence specific hybridization, or by binding to an anti-DNA antibody. The mRNA binds to the surface of a binding partner that is modified to contain oligo-dT polynucleotide. The moiety is a protein and it binds non-specifically to a binding partner modified with a detergent, preferably sodium dodecyl sulfate, Alternatively, the surface of the binding partner is modified with an antibody specific for a protein.
Preferred Cell: The target cell is a blood cell, or a cell that has been treated with drug molecule, or candidate drug molecule.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Method: The moiety is an inorganic molecule, selected from a sodium, potassium, magnesium, calcium, chlorine, iron, copper, zinc, manganese, cobalt, iodine, molybdenum, vanadium, nickel, chromium, fluorine, silicon, tin, boron, or arsenic ion. The microparticle is a plastic particle, a polystyrene microbead, a glass bead, a magnetic bead, a hollow glass sphere, a metal particle, a particle of complex composition, or a microfabricated free-standing microstructure. The chip is silicon dioxide, silicon nitride, plastic, glass, ceramic, a photoresist, or a rubber chip.

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Method: The moiety couples to the binding partner through a linker, which is preferably cleavable, e.g. by chemical, physical or enzymatic treatment. The physical force is dielectrophoresis, travelling-wave dielectrophoresis, a magnetic force, an acoustic force, an electrostatic force, a mechanical force, an optical radiation force, or a thermal convection force. The magnetic force is produced by a ferromagnetic material, or a microelectromagnetic unit. The acoustic field is effected by a standing-wave or travelling-wave acoustic field. Alternatively, the acoustic force is produced by piezoelectric material. The electrostatic force is effected by a direct current electric field. The mechanical force is fluid flow, and the optical radiation force is effected by laser tweezers. The structure built into the chip comprises microunits, each capable of effecting he physical force when energized and in combination with the external structure. The manipulation comprises transportation, focusing, enrichment, concentration, aggregation, trapping, repulsion, levitation, separation, fractionation, isolation, or linear or other directed motion of the moiety.

L49 ANSWER 26 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN **2002-205830** [26] WPIX
DNN **N2002-156780** DNC **C2002-063025**
TI Array of protein-binding agents useful for differential binding assay comprises a number of protein-binding agents attached to a solid support.
DC A96 B04 D16 **S03**
IN BEAUSOLEIL, E; CHARYCH, D; ZUCKERMANN, R N
PA (CHIR) CHIRON CORP
CYC 94
PI WO 2001094946 A2 20011213 (200226)* EN 60p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE

SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001068173 A 20011217 (200226) <--
US 2002055125 A1 20020509 (200235) <--

ADT WO 2001094946 A2 WO 2001-US18066 20010604; AU 2001068173 A AU 2001-68173 20010604; US 2002055125 A1 Provisional US 2000-209711P 20000605, US 2001-874091 20010604

FDT AU 2001068173 A Based on WO 200194946

PRAI **US 2000-209711P 20000605**; US 2001-874091 20010604

AN **2002-205830** [26] WPIX

AB WO 200194946 A UPAB: 20020424

NOVELTY - An array of protein-binding agents stably attached to a solid support (108) surface, comprising a solid **substrate** having planar surface and different protein-binding agents (I) bound it, is new. (I) comprises an anchoring segment (104) stably bound to the surface, a peptidomimetic protein-binding segment (102) and a linker segment (106) connecting and separating the other segments.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparing the array, comprising:

(a) preparing the solid **substrate** for bonding; and

(b) contacting (I) with the **substrate**; and

(2) a differential binding assay, comprising:

(a) labeling proteins in a protein-containing biological sample solution, contacting an aliquot of the sample solution with the array, and

(b) analyzing the array to determine differential binding of protein in the sample to protein-binding agent of the array;

(3) a kit for performing the differential assay of (2) comprising the novel array; and

(4) a mixed array of protein-binding agents stably attached to the surface of the solid support comprising the array which in addition comprises a number of different antibodies bound to the **substrate**

.

USE - For differential binding assay (claimed).

ADVANTAGE - The array is stable and shows long shelf life.

DESCRIPTION OF DRAWING(S) - The drawing indicates a schematic diagram of the structure of a protein-binding agent array element.

Peptidomimetic segment 102
Anchor segment 104
Linker segment 106
Solid support. 108.

Dwg.1/11

TECH UPTX: 20020424

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Components: The **substrate** comprises a metal, preferably aluminum) on the planar surface beneath the anchoring segment. The metal surface is further coated with one of a functionalized amino-modified thiol and siloxane (preferably avidin) beneath the (104). The surface is one of metal, preferably aluminum, gold or titanium, glass or plastic.

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: (106) is 2-100C aliphatic chains, polyethylene oxide or orthogonal peptidomimetic or peptide oligomer.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: (102) is a peptoid. (104) is a thiol or biotin (preferably thiol). The aminothiol or aminosilane is functionalized with a maleimide, hydrazide, aminooxy, N-hydroxysuccinimide, anhydride, aldehyde, disulfide, thiol, azide or phosphine (preferably maleimide-functionalized or avidin-functionalized). The avidin protein is avidin, streptavidin, neutravidin or its analogs. The avidin protein is attached to the metal **substrate** surface via an NHS-LC-LC-biotin moiety. The maleimide-functionalized aminothiol or aminosilane comprises a spacer. (106) is orthogonal. The maleimide-functionalized aminothiol or aminosilane comprises an NHS-LC-LC-biotin moiety. The aminosilane is aminopropylsilane.

Preferred Method: The step (a) involves spotting a droplet of a solution of (I) in a different location on the **substrate** surface under conditions such that the binding of (I) to the **substrate** is complete before the droplet evaporates. When the **substrate** surface comprises gold or aluminum coating, preparing and coating comprises cleaning the coating with the functionalized aminothiol or aminosilane. The method of making the array preferably involves generating a library of (I), distributing (I) from the library into individual storage receptacles for each different (I), preparing several (I) for binding to the solid **substrate**, and preparing the **substrate**. The differential binding assay further involves:
(a) selecting (I) based on the assay results;
(b) sequencing (102) of (I);
(c) subjecting (102) to structural analysis by mass spectroscopy;
(d) enriching the protein-containing biological sample solution with a protein which preferentially binds to the selected (I) by applying a second aliquot of the sample solution to a separation column containing a chromatography support displaying the selected (I), sequencing the enriched protein, subjecting the enriched protein to structural analysis by mass spectroscopy;
(e) contacting an aliquot of the sample solution containing labeled cDNA or messenger RNA with a DNA array;
(f) analyzing the DNA array to determine differential binding of nucleic acids in the sample to elements of the DNA array; and
(g) comparing the differential binding results of the arrays to identify correlations in gene activity and protein expression.

L49 ANSWER 27 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-195876 [25] WPIX
DNC C2002-060582
TI Fluorescently-labeled nucleic acid probes for assaying nucleic acids and their polymorphism and mutation, particularly useful in science and medicine for e.g. analytical applications, disease diagnosis and microbial identification.
DC B04 D16
IN KAMAGATA, Y; KANAGAWA, T; KURANE, R; KURATA, S; TORIMURA, M; YAMADA, K; YOKOMAKU, T
PA (DOKU-N) DOKURITSU GYOSEI HOJIN SANGYO GIJUTSU SO; (KANK-N) KANKYO ENG KK; (BIOI-N) BIOINDUSTRY KYOKAI SH; (KANK-N) KANKYO ENG CO LTD; (NAAD-N) NAT INST ADVANCED IND SCI & TECHNOLOGY
CYC 22
PI WO 2002008414 A1 20020131 (200225)* JA 152p
    RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
    W: CA US
  JP 2002000275 A 20020108 (200225) 15p
  JP 2002119291 A 20020423 (200243) 41p
ADT WO 2002008414 A1 WO 2001-IB1147 20010627; JP 2002000275 A JP 2000-193133 20000627; JP 2002119291 A JP 2001-133529 20010427
PRAI **JP 2000-292483 20000926; JP 2000-193133 20000627 ; JP 2000-236115 20000803**
AN 2002-195876 [25] WPIX
AB WO 200208414 A UPAB: 20020418
NOVELTY - Nucleic acid probes are for assaying nucleic acids by hybridizing with a target nucleic acid in which a single-stranded oligonucleotide is labeled with a fluorescent substance and a quencher in a manner that the fluorescence intensity of the hybridization reaction system is increased after completion of the hybridization but no stem loop structure is formed.

DETAILED DESCRIPTION - Nucleic acid probes are for assaying nucleic acids by hybridizing with a target nucleic acid in which a single-stranded oligonucleotide is labeled with a fluorescent substance and a quencher in a manner that the fluorescence intensity of the hybridization reaction system is increased after completion of the hybridization and no stem loop

structure is formed between the base chain at site of the labeling with the fluorescent substance and the base chain at site of the labeling with such quencher.

INDEPENDENT CLAIMS are also included for:

(1) fluorescent pigment-labeled nucleic acid probes for the determination of the concentration of target nucleic acids, the sequence of which is so designed in which the probe hybridizes with the target nucleic acid leading to a decrease in fluorescence intensity, with fluorescent labeling is at the terminal part of such probe and when hybridized the probe is 1-3 bases separated from the terminal base of the target nucleic acid with at least 1 base being G (guanine) in the base sequence of such target nucleic acid, or pairs of not less than 1 G and C (cytosine) are formed from a plurality of base pairs in the probe-nucleic acid hybrid of the terminal portion;

(2) other fluorescence-labeled nucleic acid probes for determining concentration of target nucleic acids, the base sequence of which is so designed in which the probe is for hybridization with a target nucleic acid leading to a decrease in fluorescence intensity, with fluorescence labeling at a portion other than the 5'-terminal phosphate group or 3'-terminal OH group of such probe and when hybridized pairs of not less than 1 G and C (cytosine) are formed from a plurality of base pairs in the probe-nucleic acid hybrid of the terminal portion;

(3) a method for analysis of polymorphism and/or mutation or their determination is by measuring the change in fluorescence intensity after hybridization between the probe and target nucleic acid;

(4) a method for quantitative analysis of polymorphism which is by amplification of the target gene by a quantitative target gene amplification method through the ratio of the target gene amount and that of its polymorphism;

(5) kits for determining concentration of the target nucleic acid containing or attached with the nucleic acid probes;

(6) reagent kits for quantitative polymerase chain reaction (PCR) containing, or attached with the nucleic acid probes;

(7) a device for determining the concentration of a target nucleic acid by binding the nucleic acid probes to surface of several solid supports for hybridization with the target nucleic acid with measurement of the change in fluorescence intensity, in which the nucleic acid probes are particularly arranged and bound to surface of solid supports in array shape for measuring concentration of a single or several nucleic acids;

(8) a method for determining concentration of the target nucleic acid by using the device for nucleic acid determination;

(9) a method for the analysis or determination of polymorphism or/and mutation of the target nucleic acid by using the device;

(10) a method for quantitative polymorphism analysis by using the device;

(11) a method for determining a target nucleic acid by using the nucleic acid probes, particularly as primer, for PCR and measuring the initial concentration of the amplified target nucleic acid from the degree of changes in fluorescence intensity generated by hybridization of such probes and the amplified target nucleic acid;

(12) another method for determining a target nucleic acid by using the nucleic acid probes for PCR and measuring the initial concentration of the PCR-amplified target nucleic acid from determined fluorescence intensity of the reaction system when the probe is removed by polymerase during nucleic acid elongation, or during nucleic acid mutation reaction or after completion of nucleic acid mutation reaction, and fluorescence intensity during hybridization of the nucleic acid probe and target nucleic acid or amplified target nucleic acid are compared for calculation of the change in fluorescence intensity, or by basing on the decrease in fluorescence intensity when the probes are used as primer for PCR by comparing the fluorescence intensity of the reaction systems without and with hybridization of the probes and target nucleic acid or amplified target nucleic acid;

(13) a data analysis method for the concentration of a target nucleic acid by using the fluorescence intensity of the reaction system after hybridization of the target nucleic acid and the probe and with the fluorescence intensity obtained after dissociation of the formed probe-nucleic acid hybrid complex for correction;

(14) a data analysis method for the real-time quantitative method by carrying out the hybridization and fluorescence measurement, and the results from all the cycles are combined and corrected; and

(15) an analysis method for melting curve of a target nucleic acid by using the nucleic acid probes for PCR and calculating the Tm values of the various amplified nucleic acids to carry out analysis of the melting curve of such target nucleic acid.

USE - The probes are useful for assaying nucleic acids and their polymorphism and mutation, particularly useful in science and medicine for e.g. analytical applications, disease diagnosis and microbial identification.

ADVANTAGE - The probes are convenient to use and can provide results quickly.

Dwg.0/39

TECH UPTX: 20020418

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Probes: The fluorescent substance and quencher are preferably labeled at the sites of the same nucleotide in a single-stranded oligonucleotide, particularly with a distance between bases of the labeling sites being 1-20 in base number, or ((any arbitrary integer 3-8)+10n), provided that n = an integer including 0. The single-stranded oligonucleotide has a same chain length as the target nucleic acid. Such fluorescent pigment-labeled nucleic acid probe is labeled at the 3' or 5'-terminal. 3'-terminal base in the nucleic acid probe is G or C and the 3'-terminal is fluorescent labeled; or 5'-terminal base in the nucleic acid probe is G or C and the 5'-terminal is fluorescent labeled, with hydroxyl group at the 3'-carbon of ribose or deoxyribose of 3'-terminal, or that at 3' or 2'-carbon of ribose at 3'-terminal phosphorylated, and fluorescent labeling the phosphate group at 5' or/and 3'-terminal. Oligonucleotide of such fluorescence-labeled nucleic acid probe for nucleic acid determination is preferably a chemically-modified nucleic acid, e.g. 2'-O-methyloligonucleotide and 2'-O-ethyloligonucleotide, which can also be a ribonucleotide or deoxyribonucleotide-containing chimeric oligonucleotide e.g. 2'-O-methyloligoribonucleotide and 2'-O-ethyloligonucleotide. The probes are particularly for hybridization with target nucleic acids, with measurement of the change in fluorescence intensities before and after hybridization. During the determination, higher-order structures in the target nucleic acid is disrupted under suitable conditions by heat treatment before hybridization of such target nucleic acid with the nucleic acid probe. Prior to hybridization reaction, a helper probe is added to carry out hybridization in the hybridization reaction system.

Preferred Quantitative Analysis: Such analysis is by terminal reaction fragment length polymorphism (T-RFLP), restriction fragment length polymorphism (RFLP), single-strand conformation (SSCP) or cleavase fragment length polymorphism (CFLP). The quantitative target gene amplification method is particularly quantitative PCR with use of the nucleic acid probes especially as primer, including real-time monitoring quantitative PCR.

Preferred Kits: The kits may also contain or be attached with helper probes, and which can be used to analyze or determine polymorphism or mutation of a target nucleic acid.

Preferred Device: At each of the solid support surface bound nucleic acid probe, 1 or more temperature sensors and heaters are installed on surface of the opposite side to regulate temperature of the nucleic acid probe-binding region to optimum temperature conditions.

Preferred Nucleic Acid Determinations: When carrying out the nucleic acid determination, or polymorphism or/and mutation analysis, or quantitative polymorphism analysis, the target nucleic acids are particularly isolated

from a microorganism, or animal cells, or their cell homogenate, or from complex microbial systems, or cells of symbiotic microbial system, or their cell homogenate. The PCR method in the determination is a real-time quantitative PCR method.
Preferred Data Analysis Methods: The correction calculation treatment process is based on equations involving fluorescence values from n cycles and their correction, as well as values obtained with reference samples, and optionally using the melting curve to aid analysis.

L49 ANSWER 28 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN **2002-195559** [25] WPIX
DNN **N2002-148606** DNC **C2002-060364**
TI Surface functionalized supports,useful for the analysis of nucleic acids, are prepared by coating the support surface with an initiator and polymerizing monomers containing binding sites..
DC A18 A23 A25 A89 B04 D16 P42 **S03**
IN KOEHN, H; PLUESTER, W; ULBRICHT, M
PA (EPPE-N) EPPENDORF AG
CYC 28
PI WO 2001094032 A1 20011213 (200225)* DE 27p <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: JP US
EP 1204488 A1 20020515 (200239) DE <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001094032 A1 WO 2001-EP5173 20010508; EP 1204488 A1 EP 2001-949318 20010508, WO 2001-EP5173 20010508
FDT EP 1204488 A1 Based on WO 200194032
PRAI **DE 2000-10028851 20000602**
AN **2002-195559** [25] WPIX
AB WO 200194032 A UPAB: 20020418
NOVELTY - Preparing surface functionalized supports used to produce microarrays for the immobilization of biomolecules, comprising coating the surface of the support with an initiator and bringing the coated surface into contact with a solution containing at least first group of polymerizable monomers, is new. The monomers contain binding sites to which the biomolecules (probe molecules) can bind.

DETAILED DESCRIPTION - Preparing surface functionalized supports used to produce microarrays for the immobilization of biomolecules, comprising coating the surface of the support with an initiator and bringing the coated surface into contact with a solution containing at least first group of polymerizable monomers, is new. The monomers contain binding sites to which the biomolecules (probe molecules) can bind. The conditions under which the monomer solution is brought into contact with activated support is such that the monomers under mediation via the initiator bond to the support and are polymerized to form functional polymer chains establishing a structure of neighboring functional polymer chains fixed to the support surface.

INDEPENDENT CLAIMS are also included for the following:

(1) a process for the production of microarrays by the dropwise addition of probe molecules to the surface modified support (I); and

(2) the resulting support for array-binding technology.

USE - The surface functionalized supports (I) are useful for the production of microarrays for the analysis of nucleic acids.

ADVANTAGE - The support (I) is uniformly functionalized.

DESCRIPTION OF DRAWING(S) - The drawing is a cross-sectional view of a functionalized support.
Support 100
Functionalized surface 110
Indentations 120
Polymer chains 130.
Dwg.3/3
TECH UPTX: 20020418

TECHNOLOGY FOCUS - POLYMERS - Preferred Process: The initiator is a substance activated by light, preferably benzophenone. The support is glass or plastic, preferably polystyrene, polycarbonate, polyvinylchloride or polypropylene. The support is flat and has indentations in the region to be functionalized whose form and size correspond to the distance between them and are preferably in the form of a pyramid whose tip is in the support or in the form of a cone. The glass support is silanized. A second group of monomers having essentially no binding sites for the biomolecules is polymerized with the first group at the support. The second group of monomers and their concentration are such that a required hydrophilicity and/or hydrophobicity of the copolymerized polymer is achieved. The second group of monomers comprises acrylic acid, methacrylic acid and corresponding derivatives and vinyl- or alkyl compounds, preferably polyethylene glycol, methacrylate or hydroxymethylmethacrylamide. The first group of monomers comprises acrylic acid, glycidylmethacrylate or aminoalkylmethacrylate and contain COOH-, SH-, NH2-, epoxide or thiol groups as binding sites. The microarray is prepared by coating the surface modified support with the probe molecule by spotting. The probe molecule is an oligonucleotide or antibody. The microarrays form microchips for the analysis of nucleic acids.

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L49  ANSWER 29 OF 97  WPIX (C) 2002 THOMSON DERWENT
AN   2002-171819 [22]   WPIX
DNC  C2002-053237
TI   Probes for detecting target nucleotide sequence in sample, has sequence
     that forms hairpin structure having a double-stranded segment and
     single-stranded loop collectively forming region complementary to target
     sequence.
DC   B04 D16
IN   DATTAGUPTA, N
PA   (GENE-N) APPLIED GENE TECHNOLOGIES INC
CYC  96
PI   WO 2002006531 A2 20020124 (200222)* EN   72p <--
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
            SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
     US 6380377     B1 20020430 (200235)           <--
     AU 2001073453 A  20020130 (200236)           <--
ADT  WO 2002006531 A2 WO 2001-US22166 20010712; US 6380377 B1 US 2000-616761
     20000714; AU 2001073453 A AU 2001-73453 20010712
FDT  AU 2001073453 A Based on WO 200206531
PRAI US 2001-823647    20010330; US 2000-616761   20000714
AN   2002-171819 [22]   WPIX
AB   WO 200206531 A UPAB: 20020409
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NOVELTY - An oligonucleotide probe (I) comprising a nucleotide sequence (S1) that forms a hairpin structure having a double stranded segment (DSS) and a single stranded loop (SSL), where (S1) is located with DSS only, or a portion of (S1) is located within DSS and a portion is located within SSL, collectively forming a region that is complementary to a target nucleotide sequence (TS), is new.

DETAILED DESCRIPTION - (I) comprises (S1) that forms a hairpin structure having DSS and SSL, where SSL contains at least 3 nucleotides and the DSS is formed between two complementary nucleotide sequences under suitable conditions, where (a) the DSS is formed between two perfectly matched nucleotide sequences and at least a portion of the nucleotide sequences located solely within the DSS is complementary to a TS to be hybridized with; or (b) a portion of the nucleotide sequences located within DSS and a portion the nucleotide sequences located within the single stranded loop collectively form a region that is complementary to a TS to be hybridized with.

An INDEPENDENT CLAIM is also included for:
(1) an array (II) of oligonucleotide probes immobilized on a support for hybridization analysis comprising a solid support having several immobilized probes containing at least one of (I);
(2) detecting (M1) a target nucleotide sequence (TS) in a sample; and
(3) transcribing and/or amplifying (M2) an oligonucleotide probe sequence with (I).
USE - (I) is useful for detecting TS in a sample and is also useful for transcribing and/or amplifying an oligonucleotide probe sequence (claimed).
Dwg.0/9

TECH UPTX: 20020409
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Probe: (I) preferably comprises DNA, RNA, PNA or their derivative and the portion of (S1) located within DSS and SSL is substantially complementary i.e., a perfect match to its corresponding nucleotide sequence in TS, where SSL of probe comprises 3-10 or 15 nucleotides. (I) further comprises: (a) an element, preferably a crosslinking agent that is activated by chemical or photoactive treatment, which is a furocoumarin, a macromolecule having multiple ligand binding sites which is a component of biotin-avidin binding system, or a modification that facilitates intramolecular crosslinking of (I) upon suitable treatment; (b) an element preferably the restriction enzyme cleavage site or a modification that renders (I) sensitive or resistant to nuclease digestion, where at least a portion of DSS is a duplex between a DNA strand and a RNA strand, where the DNA strand contains methylphosphonates, and at least a portion of the RNA strand is complementary to TS.
Preferred Methods: (M1) comprises contacting (I) with a sample preferably biosample containing or suspected of containing TS, at a temperature of 4-90degreesC, for 1-60 minutes and under conditions that favor intermolecular (ITER) hybridization between (I) and TS over intramolecular (ITRA) hybridization of the probe itself and assessing the intermolecular hybrid form, where the conditions that favor hybridization is achieved by controlling compositions of (I) and TS so that Tm of the ITER hybrid is higher than Tm of ITRA hybrid preferably ITER is 2degreesC higher than ITRA, and where ITER or ITRA is RNA:DNA, RNA:RNA or DNA:DNA or their derivative, preferably when ITER is RNA:DNA then ITRA is DNA:DNA hybrid and TS is detectably labeled and formation of ITER is assessed by detecting the label which is preferably a chemical, enzymatic, radioactive, fluorescent, luminescent and fluorescence resonance energy transfer (FRET) label and ITER is assessed by addition of a detectably labeled secondary probe that specifically hybridizes with a portion of ITER and detection of secondary ITER hybrid formed between secondary probe and original ITER, indicating the presence of TS in the sample and further ITER and ITRA are crosslinked after the formation of ITER but before addition of secondary probe where crosslinking is effected via addition of an agent subsequent to hybridization of the original probe with TS. The hairpin structure in (I) is formed between a DNA strand that contains methylphosphonates and RNA strand that is complementary to TS. (M2) comprises contacting (I) with the DNA sequence under suitable conditions to form a probe/DNA duplex; cleaving the ribonucleotide sequence with the portion of the nucleotide sequence complementary to the sequence by RNase H treatment to open the single stranded loop; and synthesizing a RNA sequence using a RNA polymerase that is compatible with the promoter contained within the double stranded segment of (I), where at least a portion of the single stranded loop is transcribed . The method further comprises reverse transcribing the synthesized RNA sequence into a DNA sequence for several cycles to amplify the probe sequence

L49 ANSWER 30 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-121440 [16] WPIX
CR 2002-129857 [04]; 2002-194997 [20]; 2002-214544 [27]; 2002-255509 [21]
DNN N2002-091087 DNC C2002-037135

TI Fixing or processing sample or tissue for immunohistochemistry or in situ hybridization or for rapid clinical pathology diagnosis, by exposing sample to high frequency ultrasound produced by ultrasound transducer.
DC B04 D16 S05
IN CHU, W
PA (AMRE-N) AMERICAN REGISTRY OF PATHOLOGY
CYC 1
PI US 2001053525 A1 20011220 (200216)* 33p <--
ADT US 2001053525 A1 Div ex US 1999-407964 19990929, US 2001-901121 20010710
PRAI **US 1999-407964 19990929**; US 2001-901121 20010710
AN 2002-121440 [16] WPIX
CR 2002-129857 [04]; 2002-194997 [20]; 2002-214544 [27]; 2002-255509 [21]
AB US2001053525 A UPAB: 20020513

NOVELTY - Fixing or processing (M1) a sample or a tissue involves exposing the sample or the tissue to ultrasound (US) of a frequency of at least 100 KHz, where US is produced by an US transducer.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) performing (M2) immunohistochemistry, in situ hybridization or fluorescent in situ hybridization on a solid phase or Southern, Northern hybridization, a Western annealing or an enzyme linked immunosorbent assay (ELISA), by using US at a frequency of at least 100 KHz;

(2) a system (I) comprising an US transducer, an US generator, an US sensor and a central processing unit (CPU);

(3) a robotic system (II) comprising units for moving a sample or tissue and an US transducer from a first reaction chamber to a second reaction chamber; and

(4) a system (III) for processing a sample comprising a reaction chamber, an US transducer and a CPU.

USE - M1 is useful for fixing or processing a sample or tissue using US of high frequency. (III) is useful for processing a tissue sample, a membrane filter, a tissue sample mounted on a slide, a nucleic acid chip, a microarray of a tissue or an immunochip (claimed).

The method is useful in a variety of histological, pathological, immunological and molecular techniques. US fixed and processed tissue may be used for rapid immunohistochemistry or in situ hybridization or for rapid clinical pathology diagnosis. High quality fixed tissue sections may be used for laser capture microdissection, mRNA extraction and PCR studies. High quality fixed tissue blocks may be used for high throughput tissue microanalysis of the DNA, RNA and protein target for a large series of cancer research.

ADVANTAGE - The method decreases the time for conducting histology or pathology study on tissue samples by applying US to the tissue. US-fixation method provides excellent morphologic detail and excellent preservation of a variety of protein antigens and mRNA in a few minutes. US fixed specimens are superior to routine formalin fixed tissues for the immunohistochemistry performed for short times. The method also allows preservation of high quality morphology proteins and mRNA from routine formalin fixation and processing.

The technique is fast, simple, easy to perform, versatile and enables in situ hybridization and immunohistochemistry results to be uniform throughout. The method allows use of more power without destroying cells, and therefore equates to greater speed of reaction.

DESCRIPTION OF DRAWING(S) - The figure shows a tissue in a buffer being treated with ultrasound.

Dwg.2/13

TECH UPTX: 20020308

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (M1), preferably a single piece of the sample or the tissue is placed into the transducer. A single or sideband frequency in the range of 100 KHz to 50 MHz, is produced by the transducer. Two or more US transducers are used to produce an US field such that at least a portion of the sample or tissue receives US at uniform frequency and uniform intensity. Each of the transducers

produce a range of US frequencies and a range of US intensities different from a range of US frequencies and a range of US intensities produced by at least one other transducer. The range of frequencies is applied to the sample or the tissue. Preferably, the two or more US transducers are arranged around the sample or the tissue in a two dimensional or three dimensional arrangement.
Either a transducer comprising only one head that is capable of emitting a single or wideband frequency, or a transducer comprising multiple heads, is employed in the method. The one or more multiple heads are capable of emitting a wide band frequency, or one head on the single transducer produces a frequency different from a frequency produced by a second head on the single transducer. The sample tissue is rotated or the transducer revolves around the sample or the tissue. US is produced as a continuous signal preferably as a single or wideband frequency in the range of 0.1-50 MHz. Optionally, US is produced in pulses (which vary in frequency of 0.1-50 MHz or vary in intensity) in the above mentioned frequency, and as a continuous signal, where the signal varies in frequency of 0.1-50 MHz or in intensity over time.
The sample or the tissue receives US of power at least 5 W/cm2, or receives US with a poster in the range of 5-150 W/cm2. (M1) further involves use of one or more sensors to detect one or more parameters of reflected US, such as intensity or frequency. Preferably, more than one type of sensor is used, where one sensor is an US sensor and the other sensor measures temperature. (M1) also involves use of CPU to monitor the sensor readings and to control US generator. In (M2), preferably immunohistochemistry, in situ or fluorescent in situ hybridization is performed on a solid phase such as tissue section, tissue microarray or a chip.
The Southern or Northern hybridization, Western annealing or ELISA is performed on a membrane, microarray or a DNA chip. The tissue section or the membrane receives US poster of at least 0.01 W/cm2 or 0.01-100 W/cm2. The US is used in the frequency of 100 KHz-50 MHz. Preferably, US is produced by two or more US transducers as described above.

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred System: (I) comprises more than one sensor, preferably more than one type of sensor such as an US sensor or an infrared temperature sensor. (I) also comprises more than one transducer. US sensor produces readings which are processed by CPU and US generator is controlled by CPU. US transducer generates US of a single frequency or of multiple frequencies in the range of 100 KHz-50 MHz. US transducer produces US of a power 0.01-200 W/cm2. (III) comprises more than one transducer, one or more sensors, units for heating or cooling the reaction chamber, a pump, a distributor and an unit for sampling reaction fluid. (II) further comprises an unit for moving one or more sensors from the first reaction chamber to the second reaction chamber.

L49 ANSWER 31 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-089296 [12] WPIX
CR 2001-281885 [29]; 2002-114265 [05]; 2002-121510 [11]; 2002-303742 [09]; 2002-371977 [32]
DNN N2002-065811 DNC C2002-027460
TI Device for sequentially heating and cooling fluid, useful for polymerase chain amplification, includes microfluidics channel with alternating heated and cooled zones.
DC B04 D16 Q77 S05 X25
IN SCHULTE, T H; WEIGL, B H
PA (SCHU-I) SCHULTE T H; (WEIG-I) WEIGL B H
CYC 1
PI US 2001046701 A1 20011129 (200212)* 7p <--
ADT US 2001046701 A1 Provisional US 2000-206878P 20000524, US 2001-865093 20010524
PRAI **US 2000-206878P 20000524**; US 2001-865093 20010524

AN 2002-089296 [12] WPIX
CR 2001-281885 [29]; 2002-114265 [05]; 2002-121510 [11]; 2002-303742 [09]; 2002-371977 [32]
AB US2001046701 A UPAB: 20020626
NOVELTY - Device (A) for sequentially heating and cooling a fluid, comprising a microfluidics channel that contains sample at temperature T1, and two regions at higher (T2) and lower (T3) temperatures, is new. As the sample flows through the channel its temperature is increased then lowered.

USE - The device is used for polymerase chain reaction amplification of nucleic acid, to detect one or more target sequences in clinical tests, e.g. for determination of paternity or for diagnosing genetic or infectious diseases, for preparation of DNA probes specific for unknown genes, for generating cDNA libraries for sequencing, and in analysis of mutations.

ADVANTAGE - (A) is a single-use module which is economical to manufacture and use.

DESCRIPTION OF DRAWING(S) - The drawing shows a system for polymerase chain reaction amplification and detection of a single target.

Thermocycler, including alternating heated and cooled regions 10
Main channel 32
Port for introducing DNA 36
Port for introducing polymerase and primers 38
Port for introducing extraction solution, for removing primers 43
Exit port for waste 48
Detector, particularly of fluorescence 52
Exit port for amplified DNA 54.
Dwg.3/4
TECH UPTX: 20020221
TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Device: Several different regions at T2 and T3 may be present at discrete locations in the channel, using a heating strip or element (e.g. a metal plate, radiation heater or joule heater), and a cooling element. Preferably T2 is 95 degrees C and T3 45-50 degrees C. Especially, (A) is used for polymerase chain reaction (PCR) amplification of nucleic acid (NA) and includes two microfluidics channels, one for delivering NA and the other for delivering amplification reagents, coupled to a main sinuous microfluidics channel in which a laminar flow is established (at T1), so that particles can diffuse across the laminar boundary. The laminar flow passes through alternating regions at T2 and T3, within the main channel, as required for amplification. Particularly the main channel is S shaped.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Materials: Amplification reagents are Taq polymerase, deoxynucleotide triphosphates and two primers.

L49 ANSWER 32 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-049357 [06] WPIX
DNC C2002-013903
TI Forming support-bound probes, by hybridizing support bound oligonucleotide to a probe with a sequence complementary to oligonucleotide and forming covalent bond between the probe and oligonucleotide or support.
DC B04 D16
IN LAIBINIS, P E; LEE, I H; LERMAN, L S
PA (LAIB-I) LAIBINIS P E; (LEEI-I) LEE I H; (LERM-I) LERMAN L S; (MASI) MASSACHUSETTS INST TECHNOLOGY
CYC 22
PI WO 2001083826 A2 20011108 (200206)* EN 72p <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: CA JP
US 2002028455 A1 20020307 (200221) <--
ADT WO 2001083826 A2 WO 2001-US14449 20010503; US 2002028455 A1 Provisional US 2000-201986P 20000503, US 2001-848609 20010503

PRAI **US 2000-201986P 20000503**; US 2001-848609 20010503
AN 2002-049357 [06] WPIX
AB WO 200183826 A UPAB: 20020215
NOVELTY - Linking (M1) a probe to a solid support, involves providing a solid support having an array of surface-bound oligonucleotides (I), hybridizing (I) to a probe (II) comprising a pairing oligonucleotide sequence (S) complementary to (I) and a target moiety, and forming a covalent bond between (S) and either (I) or the solid support.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a support-bound probe (IIa), comprising a capture oligonucleotide sequence covalently attached to the surface of a solid support, and a conjugate comprising a target moiety, (S) which is covalently attached to the target moiety, and a crosslinking moiety (CM) covalently bound to (S) and to either (I) or the surface of the solid support;

(2) a solid support (III) bearing an array of (IIa) on its surface, or an array of surface-bound capture oligonucleotides, where each oligonucleotide is covalently bound to CM;

(3) a probe (IIb) comprising a target moiety, an oligonucleotide sequence covalently attached to the target moiety, and CM capable of forming a covalent bond to a surface or to an oligonucleotide sequence under predetermined conditions;

(4) a conjugate primer comprising a polymerase chain reaction (PCR) primer, an oligonucleotide sequence covalently attached to the PCR primer, and CM;

(5) forming (M2) a self-assembling array of a library of target moieties, by providing a solid support having an array of surface-bound capture oligonucleotides, where each capture oligonucleotide having an unique sequence is localized at one or more defined positions on the solid support, contacting the array of the surface-bound capture oligonucleotides with a mixture of conjugates comprising a library of target moieties fused to pairing oligonucleotides with sequences complementary to the surface-bound capture oligonucleotides, and forming a covalent bond between (S) and (I) or the solid support; and

(6) producing (M3) a double-stranded DNA sequence with a single-stranded overhang, by contacting a target DNA sequence with a pair of oligonucleotide primers where one of the primer is covalently attached to a single-stranded oligonucleotide through a linking moiety, and amplifying the target DNA using PCR.

USE - The method is useful for forming surface-bound probes (claimed).

ADVANTAGE - The method does not require complex protocols, complicated protection group schemes and long preparation times.
Dwg.0/10

TECH UPTX: 20020215
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Probe: The target moiety and the PCR primer are covalently attached to (S) through a linking moiety e.g. ethylene glycol, or directly attached to (S) to form a continuous oligonucleotide sequence. CM is psoralen. The target moiety is a single-stranded or double-stranded nucleotide sequence, protein, peptide, small molecule or oligopeptide. (S) comprises 3-50, preferably 3-10 nucleotides. (III) bears at least 50, preferably 500 probes on its surface, at a probe density of 1-12x10-11 moles per cm2, preferably 3-4x10-11 moles per cm2. The array comprises a library of target moieties. CM is bound to (I) under exposure of light. The support is functionalized with multiple surface-bound capture oligonucleotides all having the same sequence, or a variety of sequences localized to a defined location on the solid support. The support is functionalized with repeating units of clusters of surface-bound capture oligonucleotides having a variety of sequences localized to a variety of defined location on the solid support. Preferred Method: Forming a covalent bond involves forming a covalent bond between CM on (S), and (I) or CM on (I), and (S). The solid support of M2 is functionalized with a library of capture oligonucleotides and is

contacted with a complementary library of pairing oligonucleotides fused to a library of target moieties. The solid support is functionalized with repeating clusters of capture oligonucleotides with unique sequences, where each cluster is contacted with a set of conjugates comprising pairing oligonucleotides capable of specifically hybridizing to each unique capture oligonucleotide sequence in the cluster, and where each cluster is contacted with a different set of conjugates comprising different targeting moieties fused to a common set of pairing oligonucleotides. The cluster comprises 2-1000, preferably 2-10 different capture oligonucleotides. The single-stranded oligonucleotide further comprises a covalently attached CM. The single-stranded oligonucleotide is attached to the PCR primer which is extended to produce the sense strand of the target DNA. The 3' end of the single-stranded oligonucleotide is attached to 5' end of the PCR primer which is extended to produce the sense strand of the target DNA.

L49 ANSWER 33 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2002-049013 [06] WPIX
DNC C2002-013643
TI Detecting single nucleotide polymorphisms, comprises applying energy gradient to sample of probe-hybridized target wild type and mutant polynucleotides, to induce selective denaturation of the duplexes.
DC B04 D16
IN PERRY, B A; RAEES, S M
PA (ANAG-N) ANA-GEN TECHNOLOGIES INC
CYC 95
PI WO 2001068919 A2 20010920 (200206)* EN 27p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001045650 A 20010924 (200208) <--
US 2002042060 A1 20020411 (200227) <--
ADT WO 2001068919 A2 WO 2001-US7906 20010312; AU 2001045650 A AU 2001-45650 20010312; US 2002042060 A1 Provisional US 2000-188534P 20000310, US 2001-804589 20010312
FDT AU 2001045650 A Based on WO 200168919
PRAI **US 2000-188534P 20000310**; US 2001-804589 20010312
AN 2002-049013 [06] WPIX
AB WO 200168919 A UPAB: 20020128
NOVELTY - Detecting single nucleotide polymorphisms (SNPs) comprising applying an energy gradient to a sample of probe-hybridized target wild type and mutant polynucleotides, to induce selective denaturation of the duplexes, is new.

DETAILED DESCRIPTION - Detecting SNPs comprising:

(a) admixing a nucleotide probe with a sample containing target wild type polynucleotide and target mutant polynucleotide, where the probe has a nucleotide sequence complementary to at least a portion of one strand of either the mutant or wild type polynucleotide;

(b) inducing hybridization between the probe and target polynucleotide to form duplexes between the probe and target polynucleotide, where the target wild type polynucleotide forms homoduplexes with wild type probes and target mutant polynucleotide forms heteroduplexes with wild type probes, while the target mutant polynucleotides form homoduplexes with mutant probes and target wild type polynucleotides form heteroduplexes with mutant probes;

(c) applying an energy gradient to the sample to induce selective denaturation of the duplexes; and

(d) detecting the presence of a single stranded polynucleotide, where the presence of more than one type of polynucleotide indicates an SNP.

USE - The method is useful for detecting SNPs, for screening several

loci derived from multiple DNA samples to be rapidly and simultaneously screened for mutation in discrete areas of specific genes, and for detecting mutations based upon the different chemical and thermal stabilities of homo- and heteroduplex DNA or cDNA fragments.

DESCRIPTION OF DRAWING(S) - The figure depicts the method of detecting single nucleotide polymorphisms.

Silica bead 11

Immobilized probe 12

Target mutant nucleic acid 13

Target wild type nucleic acid 14

Reaction cartridge 15

Eluent 16

Dwg.1/5

TECH UPTX: 20020128

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The energy gradient is a thermal or a chemical gradient. The probe and the target polynucleotides are attached to a solid support. Identification of the separated strands employs capillary electrophoresis, gel electrophoresis, high performance liquid chromatography or microfluidics. The method may also include comparing the elution time of the single strand to that of a homozygous wild type sample.

L49 ANSWER 34 OF 97 WPIX (C) 2002 THOMSON DERWENT

AN 2001-662474 [76] WPIX

CR 2000-531469 [42]; 2001-289828 [29]; 2002-413378 [38]

DNC C2001-194613

TI Separating a polynucleotide from a sample, comprises immobilizing probes with specific sequences to independent areas on a substrate surface, hybridizing polynucleotides to the probe, and heating and cooling areas on the substrate.

DC B04 D16

IN KATO, H; OKANO, K; YASUDA, K

PA (HITA) HITACHI LTD

CYC 1

PI US 2001029017 A1 20011011 (200176)* 40p <--
US 6387632 B2 20020514 (200239) <--

ADT US 2001029017 A1 Cont of US 1999-329318 19990610, Cont of US 2000-522465 20000309, Cont of US 2000-666883 20000920, US 2001-790872 20010223; US 6387632 B2 Cont of US 1999-329318 19990610, Cont of US 2000-522465 20000309, Cont of US 2000-666883 20000920, US 2001-790872 20010223

FDT US 2001029017 A1 Cont of US 6093370, Cont of US 6218126; US 6387632 B2 Cont of US 6093370, Cont of US 6218126

PRAI **JP 1999-18004 19990127; JP 1998-163213 19980611 ; JP 1998-330536 19981120; JP 1998-364059 19981222**

AN 2001-662474 [76] WPIX

CR 2000-531469 [42]; 2001-289828 [29]; 2002-413378 [38]

AB US2001029017 A UPAB: 20020711

NOVELTY - Separating (M) a polynucleotide from a sample solution (SS) involves immobilizing independent split areas on a surface of a substrate (S) separately with probes (P) having different base sequences respectively, hybridizing polynucleotides in SS separately to (P), and selectively heating a specific area of (S) to allow polynucleotide complimentarily hybridized with heated (P) to liberate from (P).

DETAILED DESCRIPTION - Separating (M) a polynucleotide from a sample solution involves:

(a) immobilizing single stranded-oligonucleotide probes each having a specific base sequence to each of a number of areas, where the areas are independent and formed on the surface of a substrate;

(b) supplying a sample solution containing polynucleotides onto the substrate;

(c) heating the sample solution up to a predetermined temperature and thereafter cooling the heated solution to hybridize each of complementary

polynucleotides separately to each of probes;

(d) replacing the sample solution above the substrate with a solution containing no polynucleotide; and

(e) heating the surface of the substrate at one area of the number of independent areas on the substrate up to a predetermined temperature, and thus denaturing only a polynucleotide being hybridized complimentarily to the probe immobilized on the area to extract the denatured polynucleotide.

An INDEPENDENT CLAIM is also included for a polynucleotide separation apparatus (I) comprising:

(a) a substrate having a number of independent areas, each of single stranded-oligonucleotide probes each having a specific base sequence being individually immobilized on each of the areas;

(b) a unit for supplying a sample solution containing polynucleotides onto the substrate;

(c) a unit for replacing the sample solution above the substrate with a solution containing no polynucleotide;

(d) a temperature control unit for heating the sample solution up to a predetermined temperature and a temperature control unit for heating (the sample solution) the surface of the substrate at only one area of the number of independent areas on the substrate to a predetermined temperature; and

(e) a unit for extracting the sample solution above the substrate.

USE - (M) or apparatus (I) for (M) are useful for polynucleotide separation (claimed). (M) or (I) are useful for selectively extracting a target polynucleotide (DNA or RNA) having a specific base sequence.

ADVANTAGE - (M) or apparatus (I) for (M) selectively extracts a target polynucleotide (DNA or RNA) having a specific base sequence rapidly with a high precision.

DESCRIPTION OF DRAWING(S) - The figure shows a general view of the configuration of a polynucleotide separation apparatus.

Dwg.23/32

TECH UPTX: 20011227

TECHNOLOGY FOCUS - COMPUTING AND CONTROL - Preferred Apparatus: (I) further comprises a unit for quantitatively detecting, separately on each of the areas, fluorescence emission intensity of a fluorescent dye with respect to each of the polynucleotides hybridized to the each probe of areas on the substrate, or intensity of autoemission fluorescence of the polynucleotides. A light having wavelengths ranging from 280-650 nm is used as an exciting light for the observation of fluorescence. (I) further comprises a unit for analyzing the temperatures of each of the areas separately based on changes of the quantitatively detected fluorescence emission intensity of the fluorescent dye attached to the individual polynucleotides hybridized separately to each of the areas of the substrate or to the surface of the substrate, or based on changes of the quantitatively detected fluorescence autoemission intensity of the nucleotide sample. (I) further comprises a unit for feedback-controlling the temperature of a specific area on the surface of the substrate separately, based on the analysis result concerning the temperature of each of the areas of the substrate obtained through the unit for detecting fluorescence emission intensity emitted from the fluorescent dye. (I) further comprises a unit for separately analyzing the temperature of each area of the substrate through a thermistor or a thermocouple. (I) further comprises a unit for separately feedback-controlling the temperature of a specific area on the surface of the substrate, based upon the analysis result on the temperature of each of the areas of the substrate obtained through the analyzing unit. (I) further comprises thin film layers or particle layers having high photoabsorbing characteristics, each layer being formed separately at each of the areas on the substrate, and a unit for selectively irradiating a convergent light to a thin film layer or particle layer at the specific area of the substrate, where the specific microarea is area-specifically heated through the photoabsorption of the light being selectively irradiated. A light having a wavelength being not absorbed by any nucleotides is used as the convergent light for heating

the microarea. Substance absorbing lights each having a wavelength longer than 400 nm is applied, sprayed or vacuum-deposited on a substrate having a number of independent areas on its surface, and each of single stranded-oligonucleotide probes each having a specific base sequence being individually immobilized to each of the areas. The exciting light used for the excitation in the fluorescent observation, the light of fluorescent observation and the convergent light for heating the microarea individually have a different wavelength from each other. (I) further comprises a microsphere having an extremely higher photoabsorbing characteristics than the substrate, a unit for capturing the microsphere floating in the solution through a light radiation pressure generated by a convergent light having a numerical aperture of equal to or more than 1.2, and a unit for moving arbitrarily the microsphere to the vicinity of the specific area on the substrate by the capturing unit through the light radiation pressure and for heating the specific area on the substrate area-specifically. (I) further comprises an array of heating element layers, each layer being attached to each of the areas of the substrate, and a unit for area-specifically heating the specific microarea by allowing one of the heating element layers to evolve heat. The substrate is in the form of capillary having, on its inner surface, a number of independent split areas, each of different nucleotide probes being immobilized on each of the areas. (I) comprises a unit for introducing a sample nucleotide solution into the capillary, a temperature control unit for hybridizing the probes to polynucleotide components in the sample solution, a unit for removing polynucleotides in the sample solution, where the polynucleotides are not hybridized to the probes on the surface of the capillary, a unit for heating a specific area of the number of areas in the capillary to denature the polynucleotide component in the sample solution, where the component has been hybridized to the probe at the area, and a unit for extracting the denatured polynucleotide component. (I) further comprises a unit for placing a drop containing no nucleotide to come in contact with only a specific area of the number of areas in the capillary, a unit for heating the capillary to denature only the sample solution component being hybridized to the nucleotide probe at the area, where the drop is in contact with the area, and unit for extracting the drop containing the denatured nucleotide component. The heating unit is capable of individually heating each of the areas to a temperature ranging from 60-95 degrees Centigrade. (I) comprises the capillary having, on its inner surface, a number of cylindrically split independent areas, each of different nucleotide probes being immobilized to each of the areas, a unit for introducing a sample solution, a washing solution and air to the capillary, a unit for individually heating each of the areas of capillary, a unit for heating the specific area of the capillary and denaturing the sample solution component being hybridized to the nucleotide probe at the area to extract the component. The substrate has a metal thin film layer on its surface, and the probes are separately immobilized through a metal oxide formed on the surface of the metal thin film layer and a crosslinking agent. The metal oxide film layer absorbs a coherent light or a light having continuous wavelength, each having a wavelength of equal to or more than 350 nm and less than 633 nm, preferably having a wavelength of equal to or more than 633 nm and equal to or less than 1053 nm. The metal oxide film layer has any oxide of a metal selected from chromium (Cr), titanium (Ti), vanadium (V), iron (Fe), cobalt (Co), nickel (Ni), molybdenum (Mo) and tungsten (W). (I) further comprises a metal surface composed of an active residue A, a linker R and a metal Me having an oxidized surface and of the formula A-R-O-Me, where the polynucleotide probes are immobilized through the active residue A. The active residue is introduced onto the oxide surface of the metal through a silane coupling agent, and the polynucleotide probes are immobilized individually through the active residue. The active residue A is a glycidoxy group, and the polynucleotide probes each have an amino group and are immobilized individually through the active residue A. (I) further comprises a unit for applying a direct current (DC) field onto the

surface of the substrate, while allowing the pH of the solution containing the sample to equal to or lower than 4 to attract nucleotide components alone to the surface of the substrate modified with nucleotide probes. (I) further comprises a unit for applying an alternating field onto the surface of the substrate. (I) further comprises a reservoir for retaining the sample solution, a substrate having a number of two-dimensionally split areas on its surface, each of the areas being modified with an oligonucleotide probe, a unit for applying an alternating or DC field individually to each of the areas of the substrate, a unit for allowing individually each of the areas of the substrate to evolve heat, and a unit for identifying an area where the hybridized cell is present and for verifying the position of a cell dyed with a marker.

L49 ANSWER 35 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-656507 [75] WPIX
DNC C2001-193071
TI Microtiter plate-based assay requiring no radioactivity and which enables automated assays of DNA oxidative stress, useful for assaying DNA, assaying DNA damage and assaying repair capacity of DNA.
DC B04 D16
IN DARE, A O
PA (DARE-I) DARE A O
CYC 1
PI US 2001031739 A1 20011018 (200175)* 13p <--
ADT US 2001031739 A1 Provisional US 1999-171309P 19991221, US 2000-741426 20001221
PRAI **US 1999-171309P 19991221; US 2000-741426 20001221**
AN 2001-656507 [75] WPIX
AB US2001031739 A UPAB: 20011220
NOVELTY - Assaying (I) DNA, comprising binding to an analysis plate both sample DNA under examination and control DNA having known abasic sites, and reacting the abasic sites with an aldehyde group specific chemical reagent (an aldehyde reactive probe (ARP) (N-aminooxymethylcarbonylhydrazino-D-biotin) reagent) to attach the ARP to abasic sites, is new.

DETAILED DESCRIPTION - Assaying (I) DNA, comprising binding to an analysis plate both sample DNA under examination and control DNA having known abasic sites, and reacting the abasic sites with an aldehyde group specific chemical reagent (an aldehyde reactive probe (ARP) (N-aminooxymethylcarbonylhydrazino-D-biotin) reagent) to attach the ARP to abasic sites, is new. The method further comprises using an Enzyme Linked Immunosorbant Assay (ELISA)-like method to detect abasic sites tagged with biotin after the reacting step. The ELISA-like method includes an avidin-biotin-complex conjugated with horseradish peroxidase or alkali phosphatase.

INDEPENDENT CLAIMS are also included for the following:

(1) quantitatively (II) assaying DNA damage comprising:

(a) binding to an analysis plate sample DNA and multiple control DNA specimens each having of known number of abasic sites;

(b) tagging aldehyde groups associated with abasic sites of the sample and control DNA;

(c) performing an ELISA-like method to obtain absorbency, optical density, and color density of the sample DNA and control DNA specimens; and

(d) comparing the sample DNA with multiple control DNA specimens to determine the number of abasic sites in the sample DNA;

(2) assaying (III) repair capacity of sample DNA comprising:

(a) treating sample and control DNA specimen with an enzyme that produces a substrate to which ARP attaches;

(b) reacting the sample and specimen DNA with ARP;

(c) tagging aldehyde groups associated with abasic sites of the sample and control DNA;

(d) performing an ELISA-like method to obtain absorbency, optical density, and color density of the sample DNA and control DNA specimens;

and
(e) comparing color, optical density, and absorbency of sample DNA with multiple control DNA specimens to determine relative enzyme activity levels of the sample and control DNA;
(3) assaying (IV) DNA comprising:
(a) binding sample and control DNA to an analysis plate to a microtiter plate using Reacti-bind (RTM) (the control DNA has a known number of abasic sites);
(b) removing the excess Reacti-bind (RTM) and unbound DNA using a Tween-20 buffered detergent (so as not to remove the bound DNA);
(c) reacting the bound DNA with an excess amount of aldehyde reactive probe (ARP) reagent;
(d) removing the excess and unreacted ARP from the analysis plate;
(e) labeling/tagging the attached ARP using a biotinylated chemical agent; and
(f) performing a calorimetric analysis to quantitatively assess the sample DNA relative to the control DNA attached to the plate;
(4) a simplified kit (V) for assaying sample DNA, comprising:
(a) an analysis plate (e.g. a microtiter plate);
(b) a number of control DNA specimens of known concentration of abasic sites;
(c) a surface treatment solution to enhance attachment of the DNA to the analysis plate;
(d) a washing detergent for removing excess material from the plate;
(e) an ARP to label or tag abasic sites while attached to the plate;
(f) a colorimetric test kit such as a kit for performing an avidin-biotin horseradish peroxidase technique; and
(g) instructions to provide a colorimetric comparison between sample DNA and control DNA;
(5) determining (VI) DNA repair capacity comprising:
(a) subjecting sample and control DNA to a substrate specific repair enzyme;
(b) tagging the product of the enzyme reaction, binding the DNA to an analysis plate; and
(c) determining the resulting number of abasic sites remaining on the analysis plate after the enzyme reaction to assay the ability of the cell to undergo DNA repair; and
(6) an apparatus (VII) that automates assaying of DNA, comprising:
(a) an analysis plate to which sample and control DNA is bound;
(b) a number of processing stations that perform process activities with respect to the analysis plate including (binding DNA to a plate, reacting DNA with an aldehyde reactive probe reagent, tagging the ARP reagent, washing the DNA with a detergent and/or incubating the sample and control DNA); and
(c) a controller that effect movement of the plate to the processing stations to perform the steps of binding to the analysis plate sample DNA and multiple control DNA specimens of known number of abasic sites, tagging aldehyde groups associated with abasic sites of the sample and control DNA, performing an ELISA-like method to obtain absorbency, optical density, and color of the sample DNA and control DNA specimens, and outputting an indication of a comparison of color density of the sample DNA relative to the control DNA specimens to indicate the number of abasic sites in the sample DNA.
USE - For assaying DNA, quantitatively assaying DNA damage and assaying repair capacity of sample DNA (claimed).
ADVANTAGE - The methods and apparatus enables automation of DNA assays for large population studies, and portable hand-held devices for quantifying DNA damage and repair capacity.
Dwg.0/5

TECH UPTX: 20011220

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Methods: The method (I) comprises reacting ARP with AP sites of DNA of cells in culture before the binding step (the sample and control DNA are tagged or labeled separately

with a the residue of the ARP reagent and then bound to the analysis plate for comparison. The control DNA is a depurination of calf thymus. The method is carried out on the sample DNA and the control DNA simultaneously to remove environmental or process variables at the comparing step. Reacti-bind (RTM) is used during the binding step. The method further includes a washing step after the binding and labeling steps. In the method (III), the treating step includes using an enzyme selected from Endonuclease III, 8-oxoguanine glycosylase (yOGG1), and human 8-oxoguanine glycosylase (hOGG1). Method (V) further comprises binding to the analysis plate a relatively high percentage of DNA contained in a solution of relatively low concentration (in the range of 1.0-10.0 nanograms of DNA per milliliter). The method (VI) further comprises subjecting the sample and control DNA to a DNA glycosylase (selected from endonuclease III, N-glycosylase, 8-oxoguanine, alkA protein, and other broad and narrow spectrum DNA glycosylase).

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Kits: The kit (V) further comprises a Reacti-bind (RTM) solution for binding DNA to the analysis plate and an avidin biotin horseradish peroxidase enzyme for comparing enzyme digestion activity relative to the sample and control DNA.
Preferred Apparatus: In the apparatus (VII) the controller effects operations of the processing stations to dispense sample and control DNA on the analysis plate, react a surface treatment agent (Reacti-bind (RTM)) with the sample and control DNA to bind them to the plate, wash the plate so as to remove excess surface treatment agent, reacting the bound DNA with an aldehyde reactive probe (ARP) (to tag or label the DNA bound to the plate), biotinylating the ARP-tagged DNA, washing excess unreacted ARP from the plate without removal of bound DNA, and outputting an indication of a calorimetric technique (an avidin-biotin horseradish peroxidase technique) to indicate the number/concentration of abasic sites in the sample DNA.

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L49  ANSWER 36 OF 97  WPIX (C) 2002 THOMSON DERWENT
AN   2001-640392 [74]   WPIX
CR   2001-640393 [72]
DNN  N2001-478789        DNC C2001-189605
TI   New carriers for gene detection, particularly useful for detecting
     validity of interferon therapy, especially in a patient infected with
     hepatitis C virus.
DC   B04 D16 S03
IN   HASHIMOTO, K; HIJITAKA, M; MISHIRO, S; OOTA, Y; HIJIKATA, M; OHTA, Y
PA   (TOKE) TOSHIBA KK; (HASH-I) HASHIMOTO K; (HIJI-I) HIJIKATA M; (MISH-I)
     MISHIRO S; (OOTA-I) OOTA Y
CYC  31
PI   EP 1136570     A2 20010926 (200174)* EN   33p <--
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR
     WO 2001071031 A2 20010927 (200174)  EN        <--
         W: ID
     JP 2001333785 A  20011204 (200202)        16p
     JP 2001333786 A  20011204 (200202)        22p
     KR 2001096612 A  20011107 (200226)            <--
     CN 1333339    A  20020130 (200231)
     CN 1333377    A  20020130 (200231)            <--
     US 2002048758 A1 20020425 (200233)            <--
ADT  EP 1136570 A2 EP 2001-302705 20010322; WO 2001071031 A2 WO 2001-JP2297
     20010322; JP 2001333785 A JP 2001-62371 20010306; JP 2001333786 A JP
     2001-62372 20010306; KR 2001096612 A KR 2001-13608 20010316; CN 1333339 A
     CN 2001-122058 20010322; CN 1333377 A CN 2001-122009 20010322; US
     2002048758 A1 US 2001-813031 20010321
PRAI JP 2001-62372     20010306; JP 2000-80955    20000322
AN   2001-640392 [74]   WPIX
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CR 2001-640393 [72]
AB EP 1136570 A UPAB: 20020524
NOVELTY - A carrier for gene detection comprising a base body and a polynucleotide immobilized on the base body, is new.

DETAILED DESCRIPTION - A carrier for gene detection comprising a base body and a polynucleotide immobilized on the base body, where the polynucleotide comprises:

(a) any one of 4 fully defined sequences of 581 base pairs (I-IV) as given in the specification;

(b) a modified polynucleotide derived from (I) by including one or several deletions, substitutions or additions at any positions except for the 455th position;

(c) a polynucleotide containing the sequence that spans from positions of 441-455 or 449-459 of (I); or

(d) the complementary strand of (a), (b) or (c), is new.

INDEPENDENT CLAIMS are also included for the following:

(1) a DNA chip comprising:

(a) a base body; and

(b) a first and a second electrodes formed on the base body; where the first electrode comprises a conductive body and at least one polynucleotide (comprising (I)) immobilized on the conductive body, and the second electrode comprises a conductive body and at least one polynucleotide (comprising (II), (III) or (IV)) immobilized on the conductive body;

(2) detecting validity of interferon therapy for an individual comprising:

(a) contacting a polynucleotide sample taken from the individual with the carrier for gene detection; and

(b) determining the nucleotide sequence of the polynucleotide in the sample by detecting the hybridization reaction between the polynucleotide sample and the polynucleotide immobilized on the carrier for gene detection; or

(c) contacting the probe polynucleotide to the carrier for gene detection, which has a polynucleotide sample taken from the individual on a substrate; and

(d) determining the nucleotide sequence of the polynucleotide sample by detecting hybridization reaction between the polynucleotide sample immobilized on the substrate and the probe polynucleotide, where the probe comprises the polynucleotide cited above;

(3) gene detecting apparatus for detecting the validity of interferon therapy comprising:

(a) the carrier for gene detection;

(b) a reaction section for containing a first polynucleotide immobilized on a base body of the carrier with a sample, which contains a second polynucleotide labeled with a marker, and putting the first and second polynucleotides under hybridization reaction condition; and

(c) a marker-detecting apparatus for detecting the marker attached to the second polynucleotide; or

(d) the carrier for gene detection;

(e) a counter electrode;

(f) a voltage application means for applying voltage between the carrier for gene detection and the counter electrode;

(g) the reaction section cited in (3a); and

(h) a measurement section for measuring an electric signal generated between the carrier for gene detection and the counter electrode, when voltage is applied by the voltage applying means after the hybridization reaction; and

(4) kits for detecting validity of interferon therapy comprising:

(a) the carrier for gene detection and a buffer solution; or

(b) the carrier for gene detection, a double strand recognizer and a buffer solution.

USE - The carrier for gene detection is useful for detecting validity of interferon therapy. In particular, the carrier is useful as a means for

predicting before treatment whether interferon therapy is valid or not for a patient infected with hepatitis C virus.
Dwg.0/11

TECH UPTX: 20011217
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Carrier: The length of polynucleotide to be immobilized on the base body is no shorter than 15 nucleotides and no longer than 30 nucleotides. The base body consists of a conductive substance. The carrier for gene detection used as an electrode. Preferred Method: The method of (2a) further comprises detecting that interferon therapy is valid for the individual if the nucleotide sequence of the sample polynucleotide determined by the determination step is that of the polynucleotide cited above, particularly (I). The method further comprises labeling the polynucleotide sample taken from the individual with a marker prior to the step of contacting the polynucleotide sample with the carrier for gene detection. The marker comprises at least one of the following: fluorescent dye, hapten, enzyme, radioisotope or electrode active substance. The detection of electrochemical change is carried out by measuring an electric signal generated between the carrier for gene detection and a counter electrode when voltage is applied between the carrier gene detection and the counter electrode. In particular, an electro-active double strand recognizer, which specifically binds to a double strand polynucleotide is added to the hybridization reaction system. The electric signal generated between the carrier for gene detection and the counter electrode is generated directly or indirectly from the electro-active double strand recognizer. The method of (2b) further comprises labeling the probe polynucleotide with a marker, prior to the step of contacting it with the carrier for gene detection. The carrier for gene detection is an electrode comprising a conductive base or substance, and the sample polynucleotide taken from the individual is immobilized on the base. Detection of the hybridization reaction is carried out by detecting electrochemical change accompanied with the hybridization reaction.

L49 ANSWER 37 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-639241 [73] WPIX
DNC C2001-189129
TI Two-dimensional array of molecules, useful for high throughput screening, bound to porous material for increased capacity and sensitivity.
DC B04 D16 L02
IN LYLES, M B
PA (LYLE-I) LYLES M B
CYC 93
PI WO 2001073125 A2 20011004 (200173)* EN 20p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN ZA ZW
US 2001044112 A1 20011122 (200176) <--
AU 2001047744 A 20011008 (200208) <--
ADT WO 2001073125 A2 WO 2001-US9430 20010324; US 2001044112 A1 Provisional US 2000-192113P 20000324, US 2001-817009 20010324; AU 2001047744 A AU 2001-47744 20010324
FDT AU 2001047744 A Based on WO 200173125
PRAI **US 2000-192113P 20000324**; US 2001-817009 20010324
AN 2001-639241 [73] WPIX
AB WO 200173125 A UPAB: 20011211
NOVELTY - Two-dimensional array (A) comprising, bound to a porous material (B), at least 100 different molecules (I), each at a different, predetermined region on the surface of (B), is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of determining a target molecule (II) by applying a (II)-containing

sample to (A), where (I) are partner molecules each able to bind to different (II) and detecting any formation of (I)-(II) complexes.
USE - (A) are useful in high throughput screens to identify targets, receptors, hybridizing sequences, antibody epitopes and other intermolecular interactions.
ADVANTAGE - Compared with known, non-porous, two-dimensional arrays, (A) has greater binding capacity for (A) (improving sensitivity of assays) and, because of its three-dimensional structure, (I) remain accessible to molecules in solution and retain their native conformation. Also interactions between the bound molecules are minimized.
Dwg.0/0

TECH UPTX: 20011211
TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Materials: (B) comprises silica, alumina and optionally boron, especially (by weight) 1-50 % alumina, 50-98 % silica and 1-5 % boron. It has mean particle size over 10 micron, density at least 96.1 kg/cubic meter and the exposed surface is at least 50, especially 95, % silica. Optionally, the surface is modified to alter its chemical properties, e.g. alteration of hydrophilicity or hydrophobicity, hydroxylation with phosphoric acid or activation with oxygen. (B) are prepared as described in US5951295.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Materials: (I) are oligonucleotides, peptides, oligosaccharides, DNA, RNA, proteins or antibodies, covalently bonded to (B).
Preferred Process: Formation of (I)-(II) complexes is detected by fluorescence, radioactivity, visible or ultra-violet spectroscopy.

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Array: The array may be made entirely of (B) or comprises a layer of (B) on a support, e.g. it is a strip of material, 300 micron thick, containing microwells formed by laser etching.

L49 ANSWER 38 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-638499 [73] WPIX
DNC C2001-188826
TI New DNA base sequencing system with compact, simple and convenient structure, useful for analyzing genes or DNAs relating to gene diagnoses or gene therapies.
DC B04 D16
IN KAMBARA, H; MIYAHARA, Y; ZHOU, G
PA (HITA) HITACHI LTD
CYC 2
PI US 2001024790 A1 20010927 (200173)* 19p <--
JP 2001258543 A 20010925 (200173) 13p <--
ADT US 2001024790 A1 US 2001-805240 20010314; JP 2001258543 A JP 2000-75384 20000317
PRAI **JP 2000-75384 20000317**
AN 2001-638499 [73] WPIX
AB US2001024790 A UPAB: 20011211
NOVELTY - A system for obtaining DNA sequence information comprising a means for supplying four kinds of deoxynucleotide triphosphate (dNTP) into a reaction vessel via independent capillaries or narrow grooves, which can be in contact with a reaction solution, by pressuring or by a liquid transfer system, is new.
DETAILED DESCRIPTION - The system is for obtaining DNA sequence information, in which pyrophosphate produced upon synthesizing a strand complementary to a template DNA is converted into adenosine triphosphate (ATP) that is reacted with luciferine in the presence of an enzyme such as luciferase and the complementary strand synthesis is monitored by detecting the resulting chemiluminescence, comprising a means for supplying four kinds of deoxynucleotide triphosphate (dNTP) into a reaction vessel via independent capillaries or narrow grooves, which can be in contact with a reaction solution, by pressuring or by a liquid

transfer system, is new.

INDEPENDENT CLAIMS are also included for the following:

(1) DNA base sequencing methods, in which the pyrophosphate produced upon synthesizing a strand complementary to a template DNA is converted into ATP;

(2) reactions chamber modules used in the system; and

(3) a DNA analyzing system, which is used in the method.

USE - The system and the method are useful for analyzing genes or DNAs relating to gene diagnoses or gene therapies.

ADVANTAGE - The present DNA base sequencing system has a compact, simple and convenient structure.

DESCRIPTION OF DRAWING(S) - The figure shows a DNA base sequencing system having one reaction vessel and deoxynucleotide triphosphate (dNTP) reagent reservoirs.

reagent reservoir 1
reagent reservoir 2
reagent reservoir 3
reagent reservoir 4
device board 5
photon multiplier tube 7
current/voltage amplifier 8
computer (data processor) 9
reaction chamber or vessel 10
capillaries 12
Dwg.1/10

TECH UPTX: 20011211

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred System: The reaction vessel and the dNTP-supply capillaries or narrow grooves are incorporated into one module as a unit. The dNTP-supply capillaries or narrow grooves can be introduced into the reaction solution from the top of the reaction vessel. The dNTP is supplied intermittently and repeatedly into the reaction vessel by controlling pressurization of each dNTP reservoir or by controlling an electric field between each dNTP reservoir and the reaction vessel addition to the pressurization. The reaction chamber module used in the system comprises at least one reaction vessel and at least four lines of capillaries or narrow grooves for reagent introduction corresponding to four kinds of dNTP The capillaries or narrow grooves having an inner diameter of less than 0.2 mm and/or a cross section area of less than 0.04 mm2, at the inlet of the reaction vessel. The reaction chamber module used in the system comprises at least one reaction vessel and at least four lines of capillaries or narrow grooves for reagent introduction corresponding to four kinds of dNTP. The capillaries or narrow grooves have an inner diameter than 0.01 mm2, at the inlet of the reaction vessel. The dNTP-containing reaction reagents can be introduced from reagent reservoirs into the reaction vessel via capillaries or narrow grooves at the bottom of the reaction vessel. A supply unit for dNTP-containing reaction reagents and the reaction vessel unit are separable and each reaction agent is alternately and repeatedly supplied from the reaction reagent supply unit installed on the top of the reaction vessel into each reaction solution via capillaries or narrow grooves. The DNA analyzing system is a detection system capable of distinguishing the position of the chemiluminescence emission. The chemiluminescence is detected by an area sensor such as a cooled charge coupled device (CCD). The means for detecting chemiluminescence comprises a chemiluminescence-detecting device, e.g. a photon multiplier tube and an avalanche photodiode, and a system in which the position of the reaction vessel is may be shifted relative to the detecting device. Reagents can be supplied without contact with the reaction vessel. The reagents are simultaneously supplied independently to different reaction vessels by an ink jet method. The system is characterized in that a DNA to be used as a template for complementary strand synthesis is immobilized onto a solid surface. The DNA base sequence is monitored by detecting the resulting chemiluminescence. The system comprises a means to remove primers and

complementary strand synthesis products or to stop the extension reaction by adding dideoxy (dd)NTPs into the reaction chambers followed by removing ddNTPs after the first sequencing process using the primers, to freshly inject primers and enzymes or the like, and to subsequently carry out the second DNA sequencing process, and providing a means to carry out this process repeatedly, if necessary. The system comprises a means in which different kinds of targets DNAs (DNA samples) are immobilized onto different solid surfaces or sectioned different cells, the designated reaction is carried out using enzymes and dNTP after hybridization with the primers, and chemiluminescence resulting from the complementary strand synthesizing reaction caused by different primers is distinguished to monitor the sequence. The DNA base sequencing system comprises a reaction vessel, reagent reservoirs each holding any one of four kinds of dNTP, means to supply dNTP into the reaction vessel at least partly consisting of a capillary or a narrow groove, pressurizing means to control the supply of the reagents, means to detect chemiluminescence emitted from the reaction vessel, and means to analyze data to obtain DNA sequence information by processing the detected data. The same kind of dNTP is added twice to assure that the reaction proceeds thoroughly.
Preferred Method: In the method of (1), the pyrophosphate produced upon synthesizing a strand complementary to a template DNA is converted into ATP, which is reacted with luciferine in the presence of an enzyme such as luciferase. Each dNTP is supplied in a previously designated order into the reaction vessel by pressurizing each dNTP reservoir in order. The complementary strand synthesis is monitored by detecting the resulting chemiluminescence to obtain DNA sequence information. The method is also characterized in that a primer, which sets a starting point of the complementary strand synthesis, is immobilized onto a solid surface. The pyrophosphate produced upon synthesizing the DNA complementary strand, which is hybridized with the primer, is converted into ATP that is reacted with luciferine, e.g. by luciferase. The DNA base sequence is monitored by detecting the resulting chemiluminescence. Different kinds of primers, which hybridize with the target DNA, are immobilized onto different solid surfaces or different cells having sectioned solid surfaces. The designated reaction is carried out using dNTP after hybridization with the target DNA, and chemiluminescence resulting from the complementary strand synthesizing reaction caused by different primers is distinguished to monitor the sequence. The primers are independently immobilized onto the surface of beads, which are spatially separated according to the kind of primer. The solids with the immobilized primers on their surface are held in cells, which are spatially separated according to the kind of primer.

L49 ANSWER 39 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-618369 [72] WPIX
DNC C2001-185129
TI New device for detecting a hybridization reaction between probe biopolymers and a sample biopolymer, for identifying useful genes or diagnosing diseases, comprises.
DC B04 D16
IN MIZUNO, K; NAKAO, M; YAMAMOTO, K; YOSHII, J
PA (HISF) HITACHI SOFTWARE ENG CO LTD; (MIZU-I) MIZUNO K; (NAKA-I) NAKAO M; (YAMA-I) YAMAMOTO K; (YOSH-I) YOSHII J
CYC 28
PI EP 1132485 A2 20010912 (200172)* EN 20p <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2001255328 A 20010921 (200172) 12p <--
US 2002022226 A1 20020221 (200221) <--
ADT EP 1132485 A2 EP 2001-105870 20010309; JP 2001255328 A JP 2000-67684 20000310; US 2002022226 A1 US 2001-802804 20010309
PRAI **JP 2000-67684 20000310**
AN 2001-618369 [72] WPIX
AB EP 1132485 A UPAB: 20011206

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NOVELTY - A device for detecting a hybridization reaction comprising a container, a temperature controller, a unit supplying a washing solution into the container, an image pickup unit, and a storage unit, is new.

DETAILED DESCRIPTION - The device comprises:

(i) a container for accommodating a biochip having a reaction region on which several probe biopolymers are separately spotted;

(ii) a temperature controller for controlling the temperature of the biochip placed in the container according to a predetermined time pattern;

(iii) a unit for supplying a washing solution into the container;

(iv) an image pickup unit for taking an image of the reaction region of the biochip in the container; (e) a controller for controlling timing for taking the image with the image pickup unit; and

(v) a storage unit for storing images taken with the image pickup unit.

An INDEPENDENT CLAIM is also included for detecting a hybridization reaction comprising:

(a) binding a sample biopolymer to the biochip having a reaction region on which probe biopolymers are separately spotted; and

(b) detecting hybridization reactions at individual spots while changing the temperature of the biochip.

USE - The device and the method is useful for detecting a hybridization reaction between probe biopolymers and a sample biopolymer. This is particularly useful in identifying useful genes or diagnosing diseases.

ADVANTAGE - The present device and method are capable of detecting and quantifying specific bindings resulting from the hybridization.

DESCRIPTION OF DRAWING(S) - The figure shows an outline of a device for detecting a hybridization reaction of a chip.

biochip 10
chip case 20
pressurized-type supplying unit 23
suction-type discharging unit 24
back-flow valve 25
back-flow valve 26
solution injection cavity 27
heat block for heating the biochip 31
heat block for heating a solution 32
thermometer for measuring temperature of the biochip 33
thermometer for measuring temperature of the solution 34
computer 40
excitation light source 50
optical filter for excitation light 51
optical filter for received light 52
optical system for received light 53
image pickup unit (cooled CCD camera) 55
controller for excitation light source 56
controller for optical filters 57
controller for image pickup 58
Dwg.2/13

TECH UPTX: 20011206

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Detecting the hybridization reaction further comprises:

(i) placing the biochip in a container;

(ii) injecting the sample biopolymer into the container;

(iii) maintaining the biochip in the container at a constant temperature; and

(iv) taking images of the reaction region of the biochip at predetermined times while running the washing solution into the container, and while changing the temperature of the biochip to a predetermined time patter. The sample biopolymer is fluorescence-labeled and the fluorescent intensities of individual spots are analyzed based on the images. The degree of the hybridization reactions between the sample biopolymer and the individual target biopolymers immobilized on the spots are detected

based on changes of a fluorescent intensity of each spot with time. The information of a temperature upon a rapid fall of the fluorescent intensity of the spot is acquired. Preferred Device: The temperature controller controls the temperature of the biochip according to a simple temperature-raising time pattern. The device further comprises a device to display changes of a fluorescent intensity of a selected spot with time.

L49 ANSWER 40 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-615371 [71] WPIX
DNC C2001-184209
TI Device for detecting biomolecular probes in a sample, comprises a capillary-like casing and an immobilized substrate which is in close proximity with casing inner surface and reduces the liquid volume.
DC B04 D16
IN JOHANN, T W; PARK, S C
PA (INCY-N) INCYTE GENOMICS INC
CYC 1
PI US 6277628 B1 20010821 (200171)* 11p <--
ADT US 6277628 B1 US 1998-165465 19981002
PRAI **US 1998-165465 19981002**
AN 2001-615371 [71] WPIX
AB US 6277628 B UPAB: 20011203

NOVELTY - A device for detecting a plurality of biomolecular probes in a sample, comprising a casing, input and output openings, a nonporous substrate immobilized in an outer surface, and a liquid sample having biomolecular probes, is new.

DETAILED DESCRIPTION - A device for detecting a plurality of biomolecular probes in a sample, comprises:

(A) a casing with input and output openings;

(B) a nonporous substrate immobilized in an outer surface contained within the casing; and

(C) a liquid sample comprising biomolecular probes contained within the casing, where:

(a) the substrate contains a plurality of regions arranged in a defined manner, each with a different plurality of immobilized binding targets; and

(b) the outer surface is in close proximity with the inner surface, to minimize the ratio of the liquid sample volume contained within the casing area, yet permits the flow of the liquid sample from the input opening, between outer and inner surface, and to the output opening.

USE - The device is useful for detecting biomolecular probes in a sample, by detecting specific binding of the probes to the immobilized targets (claimed) and the levels of different polynucleotide sequences in a sample.

ADVANTAGE - The device allows for hybridization experiments to be performed with sample volumes that are less than those used in conventional microarray hybridization experiments. The ratio of sample volume to hybridization surface area can be varied by changing the inner diameter of the capillary-like casing, or the surface area of the substrate.

DESCRIPTION OF DRAWING(S) - The figure shows the cross-sectional view of the device comprising a substrate comprising several beads.

Capillary tube 2
Bead 4
Immobilized target 6
Open ends 8,10
Dwg.1/4

TECH UPTX: 20011203

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Device: The vessel is one of the several vessels in fluid connection. The casing is a capillary tube (2) made of glass. The substrate is an elongate rod or several beads, the diameter of which is approximate to the inner diameter of the capillary-like casing. Each bead (4) or the rod is less than 1 mm,

preferably less than 10 micro meters in diameter. The substrate is made of glass, optionally surface coated with a polymer to promote immobilization of the binding targets. Furthermore, the substrate is elongate, and has a length and the regions are arranged with a linear density of greater than 1x103 or 1x106 regions/cm of the length. The ratio of the liquid sample volume contained within the casing to the outer surface area of the substrate is less than 1x10-5 m, preferably 1x10-7 m or more preferably 1x10-9 m. The immobilized binding targets and corresponding biomolecular probes comprise polynucleotides which specifically bind by hybridization.

L49 ANSWER 41 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-613199 [71] WPIX
DNN N2001-457878 DNC C2001-183336
TI Seamed type intercalators, and a method and a kit for detection of nucleic acid fragment.
DC B02 B04 D16 **S03**
PA (FUJF) FUJI PHOTO FILM CO LTD
CYC 1
PI JP 2001165894 A 20010622 (200171)* 12p
ADT JP 2001165894 A JP 1999-349285 19991208
PRAI **JP 1999-349285 19991208**
AN 2001-613199 [71] WPIX
AB JP2001165894 A UPAB: 20011203
NOVELTY - Electrochemically active seamed type intercalators for detection of double stranded nucleic acid fragment.
DETAILED DESCRIPTION - Seamed type intercalators of formula (1),
R, R1 = H atom, an optionally substituted (1-3C alkyl, 2-4C acyl, 6-20C aryl, 7-23C aralkyl having 1-3C alkyl group);
Y, Y1 = -NHCO-, -CONH-;
E, E1 = an optionally substituted ferrocenyl group;
X, Z = H or a halogen atom, a 1-6C alkyl group; and
m, n, k, p = an integer of 1-6 with a proviso m+n = 4, k+p = 8.
An INDEPENDENT CLAIM is also included a method for detection of complementary nucleic acid fragment by steps of
(1) contact of an aqueous solution or dispersion of nucleic acid fragment with and an electrochemical analytic element with fixed nucleic acid fragment(s) on one end at one or plural area of divided surface of a base plate in the presence of above mentioned intercalator to bind a complementary nucleic acid fragment immobilized on the analytical element;
(2) application of 400-600 mV potential to the analytical element; and
(3) determination of electric current between the analytical element and the seamed intercalator. Further details are disclosed in 3 claims including the detection kit.
USE - Detection of double stranded nucleic acid fragment.
ADVANTAGE - A low cost intercalator that can be easily prepared.
Dwg.0/0
TECH UPTX: 20011203
TECHNOLOGY FOCUS - BIOTECHNOLOGY - A seamed type intercalator for detection of nucleic acid fragment.

L49 ANSWER 42 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-611328 [70] WPIX
DNC C2001-182614
TI Association device for nucleic acid-based diagnostic test, isolation of nucleic acids, comprises oligonucleotide probe and solid substrate having support surface comprising association surface for linking probe to substrate.
DC A96 B04 D16
IN BELOSLUDTSEV, I Y; BELOSLUDTSEV, Y Y; HOGAN, M; IVERSON, B; POWDRILL, T
PA (GENO-N) GENOMETRIX GENOMIX INC
CYC 94
PI WO 2001066687 A1 20010913 (200170)* EN 101p <--

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000069393 A 20010917 (200204) <--

ADT WO 2001066687 A1 WO 2000-US23438 20000824; AU 2000069393 A AU 2000-69393 20000824

FDT AU 2000069393 A Based on WO 200166687

PRAI **US 2000-636268 20000810; US 2000-522240 20000309**

AN 2001-611328 [70] WPIX

AB WO 200166687 A UPAB: 20011129

NOVELTY - Association device comprises nucleic acid and polypeptide probes, or combinations of these, linked to porous solid substrate (SS). SS comprises a surface comprising an external substrate surface and several internal pores. The pore surfaces comprise an association surface (AS) which is charged with net positive or negative charge density where the pH is lower or higher than the pI of AS.

DETAILED DESCRIPTION - The device has many nucleic acid probes, polypeptide probes or their combinations linked to a porous SS which comprises a surface comprising an external substrate surface and several internal pores. The pores comprise a proximal end opening to the external surface to allow passage of fluid into a pore and the pore surfaces comprise AS. The distance between the nucleic acid probe or the polypeptide probe and the charged AS is not more than 100 Angstrom .

INDEPENDENT CLAIMS are also included for the following:

(1) making the above device, by contacting a biotinylated nucleic acid probe with streptavidin tetramer in an aqueous solution, applying the solution directly to clean porous polystyrene surface or its equivalent and incubating the probe-applied polystyrene in a humid environment for a time to allow stable absorption of the streptavidin to the polystyrene surface; and

(2) making a porous surface of an association device, by:

(a) co-polymerizing streptavidin and biotinylated nucleic acid probes into a mixture of acrylamide and bis-acrylamide or co-polymerizing streptavidin into a mixture of acrylamide and bis-acrylamide, under conditions where a porous matrix polymerizes and after polymerization adding biotinylated nucleic acid probe to the polymerized porous matrix by perfusion; or

(b) contacting a porous silica matrix with a solution of activated silane by a gas phase or fluid phase deposition.

USE - The association/hybridization device is useful for associating a nucleic acid or a polypeptide in a sample to a nucleic acid or a polypeptide probe. The method comprises contacting a test sample with the device under conditions of pH higher or lower than the pI of AS, thereby inducing a net positive or negative charge density, respectively on AS. The desired pH is established by contacting the device with an aqueous solution buffered to obtain the desired pH. The nucleic acid or polypeptide not associated with the probe are washed with a buffered aqueous solution and the wash conditions induce or maintain a net positive or negative charge density on the surface of the device. The nucleic acid or polypeptide remaining associated with the probes after the washing are removed and the non-associated sample is then detected. The device is also useful for detecting a single base pair difference between a nucleic acid in a test sample and an oligonucleotide probe. The test sample is contacted with the device under conditions that induce the substrate surface or AS to have a net positive (cationic) charge density under no salt or low salt conditions and AS is altered to an anionic environment by changing the conditions to comprises a pH that induces a net negative charge density to AS, or a neutral charge density by coating AS with a neutral or anionic polymer composition. Test sample nucleic acid not associated with a probe is removed under the altered conditions and

nucleic acid remaining hybridized to the nucleic acid probe is detected (all claimed).

The device finds application in nucleic acid-based diagnostic tests, isolation and purification of nucleic acids or polypeptides from a sample.

ADVANTAGE - The device can be used at any temperature and the kinetics of association between the oligonucleotide probe and the nucleic acid in the test sample are 10 fold more rapid than the kinetics of association under conditions when the substrate surface or AS has a neutral or net negative charge density. The device and the method can be used for association/hybridization of probes to target DNA or RNA at low bulk ion concentrations. This method is effective as the surface loading of cations on a solid support creates a hybridization surface that results in a high local cation density near the surface. The electrostatic field created on the surface of SS by AS enhances the selectivity of duplex binding due to the interaction between the mismatches in the target, the probe and the electrostatic field of the surface.

Dwg.0/18

TECH UPTX: 20011129

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Arrangement: The device further comprises an aqueous solution comprising a pH lower or higher than that of pI of AS, thereby inducing a net positive or negative charge density, respectively on AS. The net positive or negative charge density on AS induces a net positive or negative charge density in the pore space of the device and generates a thermodynamic partitioning equilibrium favorable to the movement of negatively or positively charged molecules, respectively into the pore space from the aqueous solution outside of the pores and favorable to the movement of charged molecules out of the pore space.

The thermodynamic equilibrium is favorable to the movement of negatively charged DNA, RNA or polypeptides. The positively charged AS comprises at least 1011 charges/mm2 or its charge equivalent.

Preferred Substrate: SS comprises a porous bead, a microsphere, membrane, microporous membrane, film, polytetrafluoroethylene filter, fiber, hollow fiber, fabric, polyacrylamide, polymethacylamide, methyl methacrylate, glycidyl methacrylate, dialkylaminoalkyl-(meth)acrylate, N,N-dialkylaminoalkyl(meth)acrylate, agarose, polyimid, controlled pore silica, glass, porous foam comprising poly(D,L glycolic-co-lactic acid) or poly(D,L-lactide-co-glycolide) (PLGA), porous ceramic, poly(ethylene glycol terephthalate) (PEGT) or poly(butylene terephthalate) (PBT), monodispersed carbon nanotube or its equivalent comprising patterned porous silicon, porous polystyrene, poly(styrene-divinylbenzene) (PS-DVB), plastic, plastic copolymer, polyvinyl, polypropylene, polyester, poly(vinyl alcohol) (PVA) hydrogel nanoparticle or their equivalents.

SS comprises several different nucleic acid probes arranged in spatially defined areas over the surface of the association device. The pores comprises a closed distal end and an open distal end which allows passage of fluid through the pore. Only the pore surfaces comprise AS.

The distance between the nucleic acid probe and charged surface is not more than 100 (preferably 20) Angstrom.

The nucleic acid or the polypeptide probe is 11-20 residues in length and are covalently attached to AS.

AS comprises streptavidin, imidazole, citrate, histidine or their derivatives linked to an oligonucleotide or polypeptide probe at a density of 1010 molecules/mm2. The internal pores comprise a diameter of 10-1000 Angstrom, preferably 500 Angstrom. AS comprises streptavidin, histidine or imidazole (or their derivative) and has a net positive charge density at pH lower than pH 5.5, 6.7 and 6, respectively and a net negative charge density at pH higher than the above pH values. AS comprises an amino acid or peptide linked to SS surface by its amino terminal end and an aminated oligonucleotide linked to the carboxy terminal end of the amino acid or peptide.

The peptide comprises: ((arg)n-pro)n-argn, ((arg)n-pro-gly)n-argn, or ((arg)n-gly-gly)n-argn

n = 2, 3, 4, 5 or 6.
A preferred peptide comprises: ((arg)5-pro)5-arg5,((arg)5-pro)4-arg5, ((arg)5-pro-gly)3-arg5, ((arg)5-pro-gly)4-arg5, ((arg)5-gly-gly)3-arg5 or ((arg)5-gly-gly)4-arg5.
Preferred Method: In (2), the mixture comprises 19% acrylamide and 1% bis-acrylamide. The final concentration of streptavidin is 10-6 M streptavidin tetramer.

L49 ANSWER 43 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-608987 [70] WPIX
DNN N2001-454781 DNC C2001-181250
TI Immobilization of a DNA fragment on a solid carrier surface for preparation of DNA chips without blocking processes.
DC B04 D16 **S03**
PA (FUJF) FUJI PHOTO FILM CO LTD
CYC 1
PI JP 2001178442 A 20010703 (200170)* 9p <--
ADT JP 2001178442 A JP 1999-371329 19991227
PRAI **JP 1999-371329 19991227**
AN 2001-608987 [70] WPIX
AB JP2001178442 A UPAB: 20011129
NOVELTY - DNA chips without requiring blocking process, are new.
DETAILED DESCRIPTION - Immobilization of a DNA fragment on a solid carrier surface comprises:
(i) contacting a DNA fragment having a thiol terminal group and a chain molecule having a reactive substituent capable of formation of a covalent bond with the thiol group, particularly maleimidyl, alpha , beta -unsaturated carbonyl, alpha -halocarbonyl, haloalkyl, azilydine or disulfide group, and immobilized on the solid phase carrier with one terminal; and
(ii) contacting the silane coupling agent having an amino group introduced on the surface of solid phase carrier, and a carboxylic acid activating agent, in a liquid phase.
USE - Preparation of DNA chips.
ADVANTAGE - The DNA chips do not require any blocking process.
Dwg.0/2
TECH UPTX: 20011129
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Immobilization of a DNA fragment on a solid carrier surface for preparation of DNA chips.

L49 ANSWER 44 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-602793 [68] WPIX
CR 2002-010605 [01]; 2002-453609 [48]
DNN N2001-449773 DNC C2001-178619
TI Assaying a sample for a target polynucleotide or an amplification product using an encoded bead conjugate comprising a probe and a spectral code comprising a semiconductor nanocrystal, useful in pharmacogenetic testing and forensics.
DC B04 D16 L03 **S03**
IN BRUCHEZ, M P; LAI, J H; PHILLIPS, V E; WATSON, A R; WONG, E Y
PA (QUAN-N) QUANTUM DOT CORP; (BRUC-I) BRUCHEZ M P; (LAIJ-I) LAI J H; (PHIL-I) PHILLIPS V E; (WATS-I) WATSON A R; (WONG-I) WONG E Y
CYC 94
PI WO 2001071043 A1 20010927 (200168)* EN 88p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001050937 A 20011003 (200210) <--
US 2002034747 A1 20020321 (200251) <--
ADT WO 2001071043 A1 WO 2001-US9242 20010322; AU 2001050937 A AU 2001-50937

20010322; US 2002034747 A1 Provisional US 2000-191227P 20000322, Provisional US 2000-237000P 20000929, US 2001-815585 20010322
FDT AU 2001050937 A Based on WO 200171043
PRAI **US 2000-237000P 20000929; US 2000-191227P 20000322** ; US 2001-815585 20010322
AN 2001-602793 [68] WPIX
CR 2002-010605 [01]; 2002-453609 [48]
AB WO 200171043 A UPAB: 20020812

NOVELTY - A new method (M1) for assaying a sample for a target polynucleotide or an amplification product by contacting the sample with an encoded bead conjugate comprising a probe and a spectral code comprising a semiconductor nanocrystal. The binding between the probe and target polynucleotide results in a change in fluorescence characteristics of the bead which is measured.

DETAILED DESCRIPTION - A new method (M1) for assaying a sample for a target polynucleotide or an amplification product by contacting the sample with an encoded bead conjugate comprising a probe and a spectral code comprising a semiconductor nanocrystal. The binding between the probe and target polynucleotide results in a change in fluorescence characteristics of the bead which is measured.

In detail M1, comprises contacting the sample with an unlabelled probe polynucleotide attached to a substrate. The sample is suspected of containing the amplification product, and the amplification product comprises a first label and a capture sequence. The probe polynucleotide comprises first and second complementary regions and a third region located between the first and second complementary regions, The probe polynucleotide can form a stem-loop structure in which the first and second complementary regions hybridize to each other to form a stem and the third region forms a loop. At least a part of the third region is complementary to at least a part of the capture sequence, and the probe polynucleotide can preferentially hybridize to the amplification product and therefore disrupt formation of the stem-loop structure under at least one set of hybridization conditions. The method then determines if the first label is associated with the substrate to determine if the amplification product is present in the sample.

INDEPENDENT CLAIMS are included for the following:

(1) an amplification product assay complex comprising a substrate comprising an unlabelled probe polynucleotide hybridized to an amplification product from a target polynucleotide, where the amplification product comprises a capture sequence and a label, where the probe polynucleotide comprises first and second complementary regions and a third region located between the first and second complementary regions, and further where the probe polynucleotide can form a stem-loop structure in which the first and second complementary regions hybridize to each other to form a stem and the third region forms a loop, where at least a part of the third region is hybridized to at least a part of the capture sequence, and where the stem-loop structure is not formed as a result of the probe polynucleotide being hybridized to the amplification product;

(2) a method of forming an amplification product assay complex;

(3) an amplification product assay array (A1);

(4) a kit comprising:

(a) a substrate attached to an unlabeled probe polynucleotide comprising first and second complementary regions and a third region located between the first and second complementary regions, where the probe polynucleotide can form a stem-loop structure in which the first and second complementary regions hybridize to each other to form a stem and the third region forms a loop, where at least a part of the third region is complementary to at least a part of a capture sequence of an amplification product from a target polynucleotide, where the unlabeled probe polynucleotide can preferentially hybridize to the amplification product and thereby disrupt formation of the stem-loop structure under at least one set of hybridization conditions;

(b) a reagent for incorporating a label into the amplification

product;

(c) a housing for retaining the substrate and the reagent; and

(d) instructions provided with the housing that describe how to use the components of the kit to assay a sample for the amplification product; and

(5) an article of manufacture, comprising a substrate attached to an unlabeled probe polynucleotide, where the probe comprises first and second complementary regions and a third region located between the first and second complementary regions, and the probe can form a stem-loop structure in which the first and second complementary regions hybridize to each other to form a stem and the third region forms a loop.

USE - The methods are useful in pharmacogenetic testing, forensics, paternity testing and in screening for hereditary disorders. The methods are also useful for studying alterations of gene expression in response to a stimulus. Other applications include human population genetics, analyses of human evolutionary history, and characterization of human haplotype diversity. The methods can also be used to detect immunoglobulin class switching and hypervariable mutation of immunoglobulins, to detect polynucleotide sequences from contaminants or pathogens including bacteria, yeast and viruses, for HIV subtyping to determine the particular strains or relative amounts of particular strains infecting an individual and to detect single nucleotide polymorphisms, which may be associated with particular alleles or subsets of alleles.

The methods are also useful for mini-sequencing, and for detection mutations, including single nucleotide polymorphisms (SNPs), insertions, deletions, transitions, transversions, inversions, frame shifts, triplet repeat expansion, and chromosome rearrangements. The methods can be used to detect nucleotide sequences associated with increased risk of diseases or disorders, including cystic fibrosis, Tay-Sachs, sickle-cell anemia, etc.

ADVANTAGE - The methods are useful in multiple settings where different conjugates were used to assay for different target polynucleotides. The large number of distinguishable semiconductor nanocrystal labels allows for the simultaneous analysis of multiple labeled target polynucleotides, along with multiple different encoded bead conjugates.

The assay can be implemented in a homogenous format. This allows for higher assay throughput due to fewer manipulations of the sample and decreased cross-contamination resulting in more reliable assays and less downtime from cross-contamination.

Dwg.0/15

TECH UPTX: 20011121

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In M1, the substrate is selected from a microsphere (preferred), a chip (preferred), a slide (preferred), a multiwell plate (preferred), an optical fiber, or optionally a porous gel matrix. The first microsphere comprises a first spectral code comprising a first semiconductor nanocrystal and first fluorescence characteristics.

The substrate is attached to different unlabeled probe polynucleotides having corresponding different sequences, where each of the different probe polynucleotides can form a stem-loop structure and can preferentially hybridize to a corresponding different amplification product and thereby disrupt formation of its stem-loop structure under the at least one set of hybridization conditions. Each of the corresponding different amplification products comprises a label which may be the same as or different than the first label, and the method determines if the label from each corresponding different amplification product is associated with the substrate. The amplification product is produced from an amplification process comprising a polymerase chain reaction. Alternatively, the amplification product is produced from an amplification process comprising contacting the sample with an enzyme having reverse transcriptase activity under conditions in which the enzyme can reverse transcribe RNA to DNA. The substrate is washed after the contacting and

prior to determining if the label is associated with the substrate. The sample is diluted with a medium lacking the first label after the contacting and prior to determining if the label is associated with the substrate. The target polynucleotide has multiple alleles and the method selectively determines if an amplification product produced from a subset of the alleles is present in the sample. The multiple amplification products are produced from the multiple alleles but the probe polynucleotide can selectively hybridize to the amplification product from only a subset of the alleles. The amplification product is produced from a subset of the alleles by selective amplification.

The first label comprises an agent selected from a chromophore, a lumiphore, a fluorophore, a chromogen, a hapten, an antigen, a radioactive isotope, a magnetic particle, a metal nanoparticle, an enzyme, an antibody or its binding portion or its equivalent, an aptamer or one member of a binding pair. The agent is a fluorophore. The the fluorophore is selected from a semiconductor nanocrystal, a fluorescent dye (preferred) such as fluorescein, a lanthanide chelate (e.g. europium chelate, a terbium chelate and a samarium chelate), or a green fluorescent protein.

The fluorophore is a semiconductor nanocrystal. The semiconductor nanocrystal comprises a core selected from ZnS (preferred), ZnSe, ZnTe, CdS, CdSe (preferred), CdTe, HgS, HgSe, HgTe, MgTe, GaN, GaP, GaAs, GaSb, InN, InP, InAs, InSb, AlAs, AlP, AlSb, AlS, Ge, Si, Pb, PbSe, or their alloy or their mixture. The semiconductor nanocrystal comprises a shell.

The agent is an enzyme selected from alkaline phosphatase, horseradish peroxidase, beta-galactosidase, glucose oxidase, a bacterial luciferase, an insect luciferase and sea pansy luciferase. Alternatively, the agent is selected from avidin, streptavidin, digoxigenin, or biotin. The first label is a fluorophore, and determining if the first label is associated with the substrate comprises applying a light source to the substrate that can excite the fluorophore and determining if a fluorescence emission from the fluorophore occurs from the substrate. A result of determining if the first label is associated with the probe polynucleotide is used to determine if the target polynucleotide was present in the sample prior to production of the amplification product.

The amount of the first label associated with the probe polynucleotide is determined. The amount of the first label associated with the probe polynucleotide is used to determine the amount of the target polynucleotide in the sample prior to production of the amplification product. The hybridization of each of the different probe polynucleotides to its corresponding different amplification product can be separately determined through a different identified position at which each of the different probe polynucleotides is attached to the substrate. Each of the different amplification products comprises a corresponding different label and where the hybridization of each of the different amplification products to its corresponding different probe polynucleotide can be separately determined by determining if each corresponding different label is associated with the substrate. The hybridization of each of the different probe polynucleotides to its corresponding different amplification product can be separately determined by the conditions under which it hybridizes. Each different amplification product comprises a label the same as the first label. Alternatively, each different amplification product comprises a different label.

Preferably, M1 comprises:

(a) providing a first pair of first and second primers;

(b) contacting the sample which is suspected of containing the first target polynucleotide with the first primer under conditions in which the first primer can hybridize to the target polynucleotide and can be extended to form a first primer extension product;

(c) altering the sample conditions to allow dissociation of the first primer extension product from the first target polynucleotide;

(d) contacting the sample with the second primer under conditions in which the second primer can hybridize to the first primer extension product and be extended to form a second primer extension product, where the second

primer is complementary at its 3' end to the first primer extension product at a position in the first primer extension product which is 3' to the first primer, where one of the first and second primer extension products thus formed is the first amplification product and comprises a first capture sequence and a first label;
(e) altering the sample conditions to allow dissociation of the second primer extension product from the first primer extension product;
(f) contacting the sample with a first probe polynucleotide attached to a substrate under hybridization conditions in which the first probe polynucleotide can hybridize to the first amplification product, where the first probe polynucleotide comprises first and second complementary regions and a third region located between the first and second complementary regions, and further where the first probe polynucleotide can form a stem-loop structure in which the first and second complementary regions hybridize to each other to form a stem and the third region forms a loop, where at least a part of the third region is complementary to at least a part of the first capture sequence, and where the first probe polynucleotide preferentially hybridizes to the first amplification product to thereby disrupt formation of the stem-loop structure under the hybridization conditions; and
(g) determining if the first label is associated with the first probe polynucleotide.
The first target polynucleotide is DNA or RNA. The enzyme having reverse transcriptase activity is used to form the first primer extension product from the first target polynucleotide. The first target polynucleotide is single-stranded or double-stranded. The sample is again contacted with the first and second primers after altering the sample conditions to allow dissociation of the second primer extension product from the first primer extension product to form first and second extension products. Altering the sample conditions to allow dissociation of the primer extension product from the target polynucleotide comprises heating the sample. Altering the sample conditions to allow dissociation of the second primer extension product from the first primer extension product comprises heating the sample.
The method further comprises concurrently assaying the same sample for a second amplification product from a second target polynucleotide, comprising:
(a) providing a second pair of third and fourth primers;
(b) contacting the sample which is suspected of containing the second target polynucleotide with the third primer under conditions in which the third primer can hybridize to the second target polynucleotide and can be extended to form a third primer extension product;
(c) altering the sample conditions to allow dissociation of the third primer extension product from the second target polynucleotide;
(d) contacting the sample with the fourth primer under conditions in which the fourth primer can hybridize to the third primer extension product and be extended to form a fourth primer extension product, where the fourth primer is complementary at its 3' end to the third primer extension product at a position in the third primer extension product which is 3' to the third primer, where one of the third and fourth primer extension products thus formed is the second amplification product and comprises a second capture sequence and a second label which may be the same as or different than the first label;
(e) altering the sample conditions to allow dissociation of the fourth primer extension product from the third primer extension product;
(f) contacting the sample with a second probe polynucleotide attached to a substrate, which may be the same as or different than the substrate to which the first probe polynucleotide is attached, under hybridization conditions in which the second probe polynucleotide can hybridize to the second amplification product, where the second probe polynucleotide comprises first and second complementary regions and a third region located between the first and second complementary regions, and further where the second probe polynucleotide can form a stem-loop structure in

which the first and second complementary regions hybridize to each other to form a stem and the third region forms a loop and where at least a part of the third region of the second probe polynucleotide is complementary to at least a part of the second capture sequence, and where the second probe polynucleotide preferentially hybridizes to the second amplification product to thereby disrupt formation of the stem-loop structure under the hybridization conditions; and

(g) determining if the second label is associated with the second probe polynucleotide.

The first and second amplification products are produced front a single locus. The first and second amplification products differ by a single nucleotide.

The method of (2) comprises hybridizing the amplification product to an unlabelled probe polynucleotide attached to a substrate under a first set of hybridization conditions to form an amplification product assay complex, where the amplification product comprises a first label and a first single-stranded capture and where the probe polynucleotide comprises first and second complementary regions and a third region located between the first and second complementary regions, and where the probe polynucleotide can form a stem-loop structure in which the first and second complementary regions hybridize to each other to form a stem and the third region forms a loop, where at least a part of the third region is complementary to at least a part of the capture sequence, and where the probe polynucleotide hybridizes to the amplification product and thereby disrupts formation of the stem-loop structure under the first set of hybridization conditions

Preferred Array: A1 comprises a different unlabelled probe polynucleotides attached to a substrate, where each of the different unlabelled probe polynucleotides is attached at an identifiable location on the substrate, where each of the each of the different probe polynucleotides can preferentially hybridize to a corresponding different amplification product, each of the corresponding different amplification products comprising a label that can be the same or different as the label on the other different amplification products.

In A1, each of the different probe polynucleotides comprises first and second complementary regions and a third region located between the first and second complementary regions and where each of the different probe polynucleotides can form a stem-loop structure in which the first and second complementary regions hybridize to each other to form a stem and the third region forms a loop. At least a part of the third region of each of the different probe polynucleotides is complementary to at least a part of its corresponding different amplification product. Each of the different probe polynucleotides can preferentially hybridize to its corresponding different amplification product and thereby disrupt formation of its stem-loop structure under at least one set of hybridization conditions.

Preferred Kit: The reagent is a labeled nucleotide or a labeled primer. The substrate is attached to different unlabelled probe polynucleotides, where each of the different unlabelled probe polynucleotide is attached at an identifiable location on the substrate. Each of the different probe polynucleotide can preferentially hybridize to a corresponding different amplification product and each of the corresponding different amplification products comprises a label that can be the same or different as the label on the other corresponding different amplification products. Each of the different probe polynucleotides comprises first and second complementary regions and a third region located between the first and second complementary regions and each of the different probe polynucleotides can form a stem-loop structure in which the first and second complementary regions hybridize to each other to form a stem and the third region forms a loop, where at least a part of the third region of each different probe polynucleotide is complementary to at least a part of its corresponding different amplification product. Each of the different probe polynucleotides can preferentially hybridize to its

corresponding different amplification product and thereby disrupt formation of its stem-loop structure under at least one set of hybridization conditions.
Preferred Article: The different unlabeled probes are attached to the substrate, each of the different unlabeled probes are able to form a stem-loop structure and having a different sequence.

L49 ANSWER 45 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-592537 [67] WPIX
DNN N2001-441502 DNC C2001-175785
TI Kit for detecting a mutant DNA, comprises a detection vessel containing primers of different target sequences.
DC B04 D16 **S03**
PA (KEIO-N) GH KEIO GIJUKU
CYC 1
PI JP 2001169781 A 20010626 (200167)* 16p
ADT JP 2001169781 A JP 1999-357701 19991216
PRAI **JP 1999-357701 19991216**
AN 2001-592537 [67] WPIX
AB JP2001169781 A UPAB: 20011119
NOVELTY - A kit for detecting a mutant DNA, comprising a reaction vessel in which at least two primer pairs of different target sequences are added in different wells for each primer pairs, and a recording medium in which the analytical condition by heteroduplex method is recorded, is new.
USE - For genetic diagnosis of various diseases.
Dwg.0/4

L49 ANSWER 46 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-570685 [64] WPIX
DNC C2001-169663
TI Light signals detection device for drug screening, has photodetectors to detect and differentiate signals emitted from distinct areas of probe polymers bound to solid substrate.
DC B04 D16
IN O'KEEFE, M T
PA (OKEE-I) O'KEEFE M T; (STRD) UNIV LELAND STANFORD JUNIOR
CYC 20
PI WO 2001064831 A1 20010907 (200164)* EN 34p <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
US 2002004204 A1 20020110 (200208) <--
ADT WO 2001064831 A1 WO 2001-US6661 20010228; US 2002004204 A1 Provisional US 2000-185878P 20000229, US 2001-796932 20010228
PRAI **US 2000-185878P 20000229**; US 2001-796932 20010228
AN 2001-570685 [64] WPIX
AB WO 200164831 A UPAB: 20011105
NOVELTY - A light signal detection device, comprising different probe polymer sequences bound to distinct surface areas of solid substrate (10), is new. Photodetectors (20) are positioned to detect and differentiate signals emitted from distinct areas of probe polymer sequences.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a probe molecule detection method.
USE - For use in drug screening, nucleic acid sequencing, mutation analysis in biotechnology industry, for use in forensic application, an for polymorphism screening and expression pattern determination.
ADVANTAGE - Allows identification of the signal generating binding agent using individually addressable photodetectors. Reduces or eliminates detection of radiant energy from adjacent microarray regions, by having substrate integrated photodetectors, providing high density microarray substrate. Enables reuse of the photodetector layer with different polymer layers. Improves light collection efficiency and enhances signal to noise ratio significantly, by having reduced distance between microarray and photodetector. Achieves lower limit of detection, by using microarray substrate.

DESCRIPTION OF DRAWING(S) - The drawing shows a cut-away view of a microarray substrate.
Substrate 10
Photodetectors 20.
Dwg.1/6

L49 ANSWER 47 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN **2001-559276** [63] WPIX
DNN **N2001-415728** DNC **C2001-166440**
TI Microarray used for immobilizing probes, e.g. proteins, includes sample spots comprising identical samples as control spots having predetermined position.
DC B04 D16 P34 P42 **S03**
IN TAMURA, T; YAMAMOTO, T
PA (HISF) HITACHI SOFTWARE ENG CO LTD; (TAMU-I) TAMURA T; (YAMA-I) YAMAMOTO T
CYC 28
PI EP 1132136 A2 20010912 (200163)* EN 13p
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2001249130 A 20010914 (200168) 9p <--
US 2001034027 A1 20011025 (200170) <--
ADT EP 1132136 A2 EP 2001-104785 20010227; JP 2001249130 A JP 2000-60787 20000306; US 2001034027 A1 US 2001-797918 20010301
PRAI **JP 2000-60787 20000306**
AN **2001-559276** [63] WPIX
AB EP 1132136 A UPAB: 20011031
NOVELTY - A microarray, comprising a support on which sample spots are arranged in a two-dimensional array, is new. The sample spots comprise a group of sample spots of identical samples as control spots having a predetermined position. The control spots are used for correcting spotting amount errors among sample spots of other groups, having the same positions as that of the group of control spots.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) producing the novel microarray by repeating an operation of simultaneously spotting samples on the support by using a spotting device provided with pins, in which the same samples are simultaneously spotted on the support with all of the pins of the spotting device; and
(2) correcting an inter-pin spotting amount error of a microarray, comprising:
(a) simultaneously spotting the same samples as controls on the support with all of the pins of the spotting device;
(b) measuring spotting amounts of the controls spotted with the respective pins of the spotting device to obtain correction parameters for inter-pin spotting amount errors; and
(c) correcting a measured value of each sample spot on the support by using the obtained correction parameters for the inter-pin spotting amount errors.
USE - For immobilizing probes such as DNAs, RNAs, or proteins with known sequences.
ADVANTAGE - The microarray does not have an influence on measurement results even when there is a difference of spotting amount between pins.
Dwg.0/7

L49 ANSWER 48 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-557860 [62] WPIX
DNC C2001-165962
TI Thermocycling apparatus for, e.g. amplifying nucleic acid, has lateral flow device with porous membrane between sample reservoir and wicking pad, and instrument to receive lateral flow device having temperature block.
DC B04 D16
IN BROWN, T A; CHOW, T
PA (BROW-I) BROWN T A; (CHOW-I) CHOW T; (IMAG-N) IMAGENE TECHNOLOGY INC

CYC 95
PI WO 2001066688 A1 20010913 (200162)* EN 47p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
US 2001036634 A1 20011101 (200168) <--
AU 2001043487 A 20010917 (200204) <--
ADT WO 2001066688 A1 WO 2001-US7326 20010307; US 2001036634 A1 Provisional US 2000-187919P 20000308, US 2001-801434 20010307; AU 2001043487 A AU 2001-43487 20010307
FDT AU 2001043487 A Based on WO 200166688
PRAI **US 2000-187919P 20000308**; US 2001-801434 20010307
AN 2001-557860 [62] WPIX
AB WO 200166688 A UPAB: 20011026

NOVELTY - A thermocycling apparatus including a lateral flow device containing a sample reservoir, a wicking pad, and a porous membrane located between and contacting the sample reservoir and the wicking pad, is new. It also includes an instrument for receiving the lateral flow device, including a temperature block having stationary thermal zones.

DETAILED DESCRIPTION - A thermocycling apparatus including a lateral flow device, and an instrument for receiving the lateral flow device, is new. The lateral flow device comprises a sample reservoir at the proximal end of the device, a wicking pad at the distal end of the device, and a porous membrane located between and contacting the sample reservoir and the wicking pad. The instrument for receiving the lateral-flow device comprises a temperature block (6) having stationary thermal zones. The temperature block is arranged to fit between the sample reservoir and the wicking pad and in contact with the porous membrane.

An INDEPENDENT CLAIM is also included for amplifying nucleic acid, comprising:

(a) applying a nucleic acid amplification reaction mixture to the proximal end of a porous membrane; and

(b) allowing the reaction mixture to travel towards the distal end of the porous membrane, in which the reaction mixture travels through proximal stationary zones in contact with the porous membrane.

USE - For thermocycling a reaction mixture in a continuous flow. It is particularly applicable in nucleic acid amplification, concentration, and detection.

ADVANTAGE - The invention reduces the number of steps, and thus the time and skill needed to perform a polymerase chain reaction. It also reduces the instrumentation and costs per test.

DESCRIPTION OF DRAWING(S) - The drawing shows thermally conductive bars that generate temperature zones.

Thermally conductive bar 6
Heater 7
Teeth 8.
Dwg.3/4

TECH UPTX: 20011026

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Components: The lateral flow device is disposable. The porous membrane comprises a proximal amplification zone, and a distal detection zone comprising a test line zone. The detection zone comprises a test line zone and a control line zone, in which the test line zone is located distal to the amplification and the control line zone is located distal to the test line. The test line zone comprises a linear array of amplicon-capturing agent on the porous membrane. The control line zone comprises a linear array of a probe-capturing agent on the porous membrane. Each of the stationary thermal zones comprises thermally conductive bars, heaters, and temperature controllers. Each of the thermally conductive bars contains teeth and is at a different reaction temperature. The teeth are

interdigitated and do not touch each other. Preferably, the thermally conductive bars comprise a melting bar, an extension bar, and an annealing bar, and are arranged at 0 degrees, 90 degrees, and 180 degrees, with respect to each other.

L49 ANSWER 49 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-536574 [59] WPIX
DNC C2001-159787
TI Simultaneously performing many different reactions by filling a channel having reagents on wall portion of reaction regions, with liquid medium and promoting reactions between reagents in the medium and the regions.
DC B04 D16
IN ALBAGLI, D; ANDERSON, R; CAO, L; HOOPER, H H; SINGH, S; ZENG, S; SHARAT, S
PA (ACLA-N) ACLARA BIOSCIENCES INC; (ALBA-I) ALBAGLI D; (ANDE-I) ANDERSON R; (CAOL-I) CAO L; (HOOP-I) HOOPER H H; (SING-I) SINGH S; (ZENG-I) ZENG S
CYC 94
PI WO 2001061041 A2 20010823 (200159)* EN 61p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001038325 A 20010827 (200176) <--
US 2002058329 A1 20020516 (200237) <--
ADT WO 2001061041 A2 WO 2001-US4884 20010216; AU 2001038325 A AU 2001-38325 20010216; US 2002058329 A1 Provisional US 2000-183626P 20000218, US 2001-788209 20010216
FDT AU 2001038325 A Based on WO 200161041
PRAI **US 2000-183626P 20000218**; US 2001-788209 20010216
AN 2001-536574 [59] WPIX
AB WO 200161041 A UPAB: 20011012
NOVELTY - Bulk-phase medium containing reactants is added to a channel having a structure defining an elongate/planar channel and a port for introducing the medium into the channel, and a reaction-specific reagent (RSR) releasably carried on wall portion of each reaction region (RR). On release of RSR from the walls of RR, different reagent-specific solution-phase reactions occur simultaneously in each RR.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a device (12) for carrying out several different reactions in a single bulk-phase reaction medium, comprising a structure defining an elongate/planar channel (18) and a port (24) for introducing such bulk-phase medium into the channel, several discrete RRs (20,22) within the channel and a RSR releasably carried on a wall portion of each RR, for reacting in solution with one or more reagents in the bulk-phase medium, when such medium is introduced into the channel, to effect a selected solution-phase reaction in each region, and where the channel is dimensioned to substantially prevent convective fluid flow among the RRs during such reactions; and

(2) performing several affinity determinations to determine the biological activity of candidate compounds employing an elongated channel having a cross-section of 10 mu m2-4 mm2 and several sites at which a first component of the affinity determination are non-diffusively bound, where each site is bordered by a source trench and a drain trench for moving components of the affinity determination to and away from the site and the affinity determination comprising the binding of a candidate compound to an enzyme and employing an enzyme substrate which results in a detectable product, involves:

(a) electrokinetically moving each of candidate compounds from each of source trenches to each of their respective sites and incubating the resulting mixture at each site;

(b) adding the substrate to the main channel;

(c) incubating the resulting mixture at each site, resulting in a detectable product, electrophoretically moving the detectable product from the site to drain trench; and

(d) detecting detectable products separate from other components of affinity determination as a measure of the affinity determination, where the length of the site and cross-section of the channel are chosen to have a reaction volume for affinity determination of less than 100 nl.

USE - The method and device are useful for carrying out simultaneous sequence-specific nucleic acid reactions on several different DNA targets contained in the bulk-phase medium, where RSR are nucleic acid oligomer reagents releasably bound to the wall portions through duplex formation with immobilized complementary-sequence oligonucleotides or by ligand attachment to an immobilized antiligand.

The sequence-specific nucleic acid reactions include:

(1) polymerase extension reactions, where RSR in each region include extension primers;

(2) polymerase chain reaction (PCR) reactions in the RR, where RSR include one or more sets of PCR primers; or

(3) sequence-specific 5' exonuclease reactions that result in the formation of a detectable product, where RSR in each region includes as an exonuclease substrate, an oligonucleotide having a selected nucleic acid sequence terminating in a detectably labeled 5' nucleotide.

The detectably labeled 5' nucleotides associated with different RRs are electrophoretically separable (all claimed).

The method is useful for various protocols involving nucleic acid sequencing, nucleic acid hybridization, single nucleotide polymorphism detection, proteomics, specific binding pair reaction and enzyme reactions.

ADVANTAGE - For carrying out simultaneous polymerase chain reaction (PCR) reactions, the method minimizes the possibility of specious amplification products formed by mismatched primers, since each reaction is carried out substantially in the presence of one primer set only. The reaction in each region can be carried out to higher amplicon levels, since the concentration of a single primer pair in each region is relatively high.

The amplicon products can be detected directly in isolated form, by capture of labeled amplicon strands on the wall portion of each RR. The possibility of false positives, due to primer mismatches, is reduced because only a single primer pair is present in each RR. The amount of signal produced is enhanced because of the greater concentration of a single primer or primer set in each RR. Finally, the reaction products are detected in situ, by electrophoresis of reaction products through the device channel or by analyzing individual reaction components in the bulk-phase solution.

DESCRIPTION OF DRAWING(S) - The figure shows the sectional view of the device for carrying out several different reactions in a single bulk-phase reaction medium.

Device 12
Substrate 14
Covering 16
Channel 18
Input port 24
Output port 26
Reaction regions 20,22
Dwg.1B/12

TECH UPTX: 20011012

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: After the completion of the reactions, the medium is removed from the device for analysis or processing of the several reaction products.

The bulk-phase medium contains different DNA targets and RSR in the different RRs include polymerase chain reaction primers (PCR) primers, designed to hybridize with and amplify different, selected regions of the DNA targets. The reaction is promoted by successively heating and cooling

the device, under conditions effective to produce PCR amplicons.
Preferred Device: The channel defining structure defines a one-dimensional channel having a substantially uniform cross-section along its length, channel width and depth dimensions between 20-800 mum and RR is submicroliter in volume.
Alternatively, the channel has several cross-sectionally bulged regions corresponding to RR and connected in series by channel sections having channel width and depth dimensions between 20-800 mum. The structure includes a pair of planar expanses that are separated from one another by a dimension between 20-800 mum. Each RR includes a capture nucleic acid immobilized on the associated wall portion and has a region-specific nucleic acid sequence.
Different sequence nucleic acid oligomer reagents are hybridized with such capture nucleic acids. The device comprises a substrate (14) defining an elongate channel terminating at first and second ends and a lid covering the open channel to form an elongate closed channel terminating at the ports. The substrate is designed to be placed in a centrifugation apparatus, such that centrifugation of the device is effective to cause liquid medium introduced at one port to fill the channel or liquid medium contained within the channel to be expelled from it.

L49 ANSWER 50 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-522613 [57] WPIX
DNC C2001-156071
TI Conducting simultaneous micro volume reactions in biochemical reactor, involves using sample chamber which holds sample film.
DC B04 D16
IN FOREMAN, P K; O'KEEFE, M; O'KEEFE, M T
PA (STRD) UNIV LELAND STANFORD JUNIOR; (FORE-I) FOREMAN P K; (OKEE-I) O'KEEFE M
CYC 94
PI WO 2001061054 A2 20010823 (200157)* EN 65p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001038606 A 20010827 (200176) <--
US 2001055765 A1 20011227 (200206) <--
US 2002072096 A1 20020613 (200243) <--
ADT WO 2001061054 A2 WO 2001-US5550 20010220; AU 2001038606 A AU 2001-38606 20010220; US 2001055765 A1 Provisional US 2000-229357P 20000218, US 2001-789899 20010220; US 2002072096 A1 Provisional US 2000-229357P 20000218, US 2001-789601 20010220
FDT AU 2001038606 A Based on WO 200161054
PRAI **US 2000-229357P 20000218**; US 2001-789899 20010220; US 2001-789601 20010220
AN 2001-522613 [57] WPIX
AB WO 200161054 A UPAB: 20011005
NOVELTY - Conducting simultaneous micro volume reactions, comprising introducing liquid samples in sample chambers of micro hole apparatus and samples contain reaction components. The micro hole apparatus has a substrate through which each chamber extends. The chamber holds the film of sample within walls so as to prevent mixing with another sample. The chamber has height width ratio which is less than 1:1.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) method of adding component to micro volume reaction;
(2) method for adding nucleic acid to micro volume reaction;
(3) method for introducing liquid sample to sample chamber;
(4) method for diluting a solution;
(5) method for selective retention of molecule;

(6) method for simultaneously desalting solution;
(7) method for selective retention of nucleic acid;
(8) method for parallel electrophoretic analysis of plurality of micro volume reaction;
(9) method for preparing samples for mass spectrometric analysis;
(10) method for mixing micro volume samples;
(11) apparatus for containing multiple micro volume liquid samples;
(12) kit comprising apparatus for containing multiple micro volume liquid samples; and
(13) method for simultaneously conducting micro volume polynucleotide amplification reaction.

USE - In biochemical or biological reactor nucleotide sequencing, amplification reaction, enzyme digestion, ligation, primer extension, enzyme medical reaction, hybridization reaction.

ADVANTAGE - Use of sample chamber enables high output, ease of handling, performance of low volume reaction, rapid thermal cycling and optical access to samples.
Dwg.0/7

L49 ANSWER 51 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-522607 [57] WPIX
DNC C2001-156065
TI Parallel genotyping of samples from multiple patients by direct sample immobilization onto microspheres of array, contacting array with readout probes and detecting presence of target analyte.
DC B04 D16
IN CHEE, M S; FAN, J
PA (ILLU-N) ILLUMINA INC; (CHEE-I) CHEE M S; (FANJ-I) FAN J
CYC 94
PI WO 2001061043 A2 20010823 (200157)* EN 59p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001038389 A 20010827 (200176) <--
US 2002001801 A1 20020103 (200207) <--
ADT WO 2001061043 A2 WO 2001-US5027 20010216; AU 2001038389 A AU 2001-38389 20010216; US 2002001801 A1 Provisional US 2000-182955P 20000216, US 2001-785514 20010216
FDT AU 2001038389 A Based on WO 200161043
PRAI **US 2000-182955P 20000216**; US 2001-785514 20010216
AN 2001-522607 [57] WPIX
AB WO 200161043 A UPAB: 20011005
NOVELTY - Parallel genotyping (GT) of multiple patients comprises providing an array composition comprising a substrate (S) with a surface having discrete sites and a population of microspheres (MS) distributed on the surface, where MS comprise two subpopulations, each having several target analytes, contacting the array with a set of readout probes and detecting the presence of target analyte.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an array composition comprising a (S) with a surface comprising discrete sites and a population of MS comprising two subpopulations, each comprising several target analytes, where the MS are distributed on the surface.

USE - The method is useful for parallel genotyping of multiple patients and for determining the identification of a nucleotide at the detection position in a target sequence (claimed). The array is useful for detecting and analyzing genotypes, single nucleotide polymorphisms and the presence or absence of subsequences such as genes in a sample for e.g. the presence or absence of chromosomal aberrations such as deletions or duplications in tumor samples. In addition, the method is useful for

quantitation of the amount of target sequence.
ADVANTAGE - The method facilitates parallel analysis of a large number of sample components from a large number of patients.
Dwg.0/4

TECH UPTX: 20011005
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The method further comprises contacting the array composition with a second set of readout probes and detecting the presence of second target analyte. The first set of readout probes comprises a first and second readout probes, which comprises first and second label, respectively. The method further comprises detecting the first label as an indication of the presence of the first target analyte. The two subpopulations each comprise several target analytes from different patients.
Parallel GT can also be carried out by contacting an array composition comprising (S) and a population of MS comprising two subpopulations, each comprising target analytes attached to MS with attachment groups with a set of extension probes that hybridize with a target sequence adjacent to a detection position to form an extension complex. The extension complex is contacted with a composition comprising a first nucleotide and polymerase which extends the extension probe with the nucleotide when the nucleotide is complementary to the detection position of the target sequence and the presence of nucleotide is detected.
A hybridization complex is formed between the target sequence and the readout probe. The method further comprises contacting the hybridization complex with a first nucleotide comprising a label and a polymerase which extends the readout probe with the nucleotide when the nucleotide is complementary to the detection position of the target sequence. The target sequence comprises two target domains, where the hybridization complex comprises the target sequence, a readout probe hybridized to the first domain and second readout probe hybridized to the second domain and the nucleotide at the detection position is determined by adding a ligase to form a ligation complex.
Preferred Array: (S) is a fiber optic (S) or plastic and the discrete sites are wells. MS of each subpopulation further comprise an optical signature and identifier binding ligand, such as nucleic acid. MS are randomly distributed on the surface. MS of the two subpopulation each comprise several target analytes from the two target sources. The target analytes are nucleic acids comprising genomic DNA, or proteins.

L49 ANSWER 52 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-517725 [57] WPIX
DNN N2001-383625 DNC C2001-155011
TI Detecting complementary nucleic acid fragments by superposing a DNA microarray containing a hybridized sample onto a sheet with a fluorescent material that is radiation permeable at specific locations.
DC B04 D16 **J04 S03**
IN NERIISHI, K; OGURA, N; TAKAHASHI, K; UMEMOTO, C
PA (FUJF) FUJI PHOTO FILM CO LTD; (NERI-I) NERIISHI K; (OGUR-I) OGURA N; (TAKA-I) TAKAHASHI K; (UMEM-I) UMEMOTO C
CYC 2
PI JP 2001183371 A 20010706 (200157)* 9p <--
US 2002076701 A1 20020620 (200244) <--
ADT JP 2001183371 A JP 1999-372976 19991228; US 2002076701 A1 US 2000-749791 20001228
PRAI **JP 1999-372976 19991228**
AN 2001-517725 [57] WPIX
AB JP2001183371 A UPAB: 20011005
NOVELTY - Detecting complementary nucleic acid fragments by superimposing a DNA microarray containing a hybridized sample onto a sheet with a fluorescent material that is radiation permeable at specific locations, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a kit for detecting complementary nucleic acid fragments comprising (I) fixed to a support body (13) and (II);
(2) a laminate for detecting complementary nucleic acid fragment which comprises (I) aligned with (II);
(3) storage property fluorescent material sheet (II) for detecting complementary nucleic acid fragment, present on support body (15).
USE - Detecting complementary nucleic acid fragments using DNA microarray and autoradiography, for research purposes, in gene analysis, and in medical fields.
ADVANTAGE - The image formed by radiation has a high resolving degree and sharpness. Accurate gene analysis can be performed in a short time using the DNA microarray as described above.
DESCRIPTION OF DRAWING(S) - The figure shows the DNA microarray used in autoradiography purposes for detecting complementary nucleic acid fragments.
DNA microarray 11
Storage property fluorescent material sheet 12
Support body of DNA microarray 13
Support body of storage property fluorescent material sheet 15
Storage property fluorescent material layer 16
Storage property fluorescent material area 18
Dwg.1/4

TECH UPTX: 20011005
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Nucleic Acid: (I) comprises several kinds of multiple single stranded (ss) nucleic acid fragments fixed to a supporting unit. The same kind of multiple ss-nucleic acid fragments are fixed at points away from the different kinds of multiple ss-nucleic acid fragments. Preferred Method: The detection method comprises:
(i) contacting the sample ss-nucleic acid fragment labeled by radioactive substance, in liquid phase, with (I), in order to bind the sample ss-nucleic acid fragment with the complementary sequence by hybridization;
(ii) removing unbound sample ss-nucleic acid fragment from (I);
(iii) superposing (I) with a storage property-fluorescent material sheet (II) (12), at positions (18) corresponding to (I); and where the fluorescent material part can accumulate radiation emitted from radioactive label of the sample ss-nucleic acid fragment fixed to (I);
(iv) irradiating light on (II) which accumulates the radiation and exhibits fluorescence;
(v) condensing the longer wavelength light emitted by (II) and converting it into electrical signal by photoelectric conversion; and
(vi) detecting the position of bonded ss-nucleic acid fragment.
Preferred Fluorescent Sheet: (II) comprises a radiation impermeable material at positions corresponding to the positions of (I) which does not comprise the fixed ss-nucleic acid fragment.

L49 ANSWER 53 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-515425 [57] WPIX
DNC C2001-154220
TI Device for carrying out immunocytochemical protocols and in situ hybridization on microscope slide has narrow gap between cover plate with liquid inlet and outlet and slide, allowing liquid to be fed over sample on slide.
DC A96 B04 D16
IN GAUSEPOHL, H
PA (GAUS-I) GAUSEPOHL H
CYC 1
PI DE 10004801 A1 20010809 (200157)* 5p <--
ADT DE 10004801 A1 DE 2000-10004801 20000203
PRAI **DE 2000-10004801 20000203**
AN 2001-515425 [57] WPIX
AB DE 10004801 A UPAB: 20011005
NOVELTY - Device for carrying out immunocytochemical protocols, in situ

hybridization and related processes on biological material on a microscope slide has a narrow gap (5) between a cover plate (1) with liquid inlet and outlet (3, 4) and the slide, which is optionally fitted with a seal (6). This allows liquid to be fed over a sample on the slide.

USE - For carrying out immunocytochemical protocols, in situ hybridization and related processes on biological material.

ADVANTAGE - Different liquids can be fed over the sample without opening the device, allowing automated operation.

DESCRIPTION OF DRAWING(S) - The drawings show plan and side views of the device.

Cover plate 1

Liquid inlet and outlet 3, 4

Narrow gap 5

Seal 6

Dwg.1/1

TECH UPTX: 20011005

TECHNOLOGY FOCUS - POLYMERS - Preferred Apparatus: The seal is made from polyolefin, polytetrafluoroethylene, silicone, polyvinyl chloride or rubber. The cover plate is made from glass, ceramic, polytetrafluoroethylene, polyolefin, polysulfone or silicone.

L49 ANSWER 54 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-514426 [56] WPIX
DNN N2001-381089 DNC C2001-153697
TI Apparatus for hybridization assays and disease diagnostics, comprises probes immobilized on a flexible elongated substrate.
DC A89 B04 D16 **J04 S03**
IN CHEN, A C; CHEN, S; LUO, Y
PA (GENO-N) GENOSPECTRA INC; (CHEN-I) CHEN S; (LUOY-I) LUO Y
CYC 94
PI WO 2001051207 A1 20010719 (200156)* EN 114p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001027868 A 20010724 (200166)
US 2001051714 A1 20011213 (200204) <--
ADT WO 2001051207 A1 WO 2001-US1026 20010110; AU 2001027868 A AU 2001-27868 20010110; US 2001051714 A1 Provisional US 2000-175225P 20000110, Provisional US 2000-190495P 20000320, Provisional US 2000-227874P 20000825, Provisional US 2000-244418P 20001030, US 2001-758873 20010110
FDT AU 2001027868 A Based on WO 200151207
PRAI **US 2000-244418P 20001030; US 2000-175225P 20000110 ; US 2000-190495P 20000320; US 2000-227874P 20000825;** US 2001-758873 20010110
AN 2001-514426 [56] WPIX
AB WO 200151207 A UPAB: 20011001

NOVELTY - A novel apparatus (I) for sample identification with probes, comprises a flexible elongated substrate and several different probes immobilized on discrete areas of a probe-containing substrate surface, where each area contains one probe.

DETAILED DESCRIPTION - The substrate in (I) is three dimensional (3D).

INDEPENDENT CLAIMS are also included for the following:

(1) apparatus (II) or sample identification with probes comprising a substrate, several different probes immobilized on discrete areas of a probe-containing substrate surface, where each area contains one probe, and two markers conveying information about two respective sets of probes;

(2) apparatus (III) for binding a target molecule to an immobilized probe, comprising a coiled flexible probe carrier and several immobilized probes;

(3) apparatus (IV) for depositing probes on a substrate, comprising a reservoir with an array of wells and a set of capillaries which each have two ends so that one end is connected to a well allowing well contents to enter the capillary, and the other end is arranged to form a flat row with all other ends of all the capillaries;

(4) fabricating (M1) a probe carrying apparatus comprising:

(a) depositing probes onto a flexible, elongated 3D substrate (M1a); or

(b) depositing a liquid containing a prone, by painting a strip on a 3D substrate and repeating for a second liquid on a second strip (M1b);

(5) hybridizing (M2) a target molecule to an immobilized probe, comprising contacting at least one of several probes immobilized on a wound flexible elongated probe carrier, with a hybridization fluid;

(6) reading (M3) a hybridization result comprising M2 and imparting rotational motion to the probe carrier member about a longitudinal axis of the carrier, and a relative translational motion along the same axis between the carrier and a reader head;

(7) reading (M4) a hybridization result comprising M2 and imparting rotational motion to the probe carrier on a planar disc member about a longitudinal axis of the carrier, and a relative translational motion along the same axis between the disc and a reader head along a radial direction of the disc; and

(8) reading (M5) a hybridization result comprising hybridizing the target molecule to the probe by M4, and unspooling the carrier to draw the probe carrier past a reader head;

(9) reading (M6) a hybridization result comprising hybridizing the target molecule to the probe by M2-4, and detecting the presence of the target molecule.

USE - (I) is used to detect the presence of target molecules in a hybridization fluid (claimed). (I) is used to construct probe arrays, large-scale hybridization assays (e.g. fingerprinting, mutational, linkage and polymorphism analyses, and sequencing), disease diagnostics, microorganism or mutation identification and gene mapping.

DESCRIPTION OF DRAWING(S) - The figure shows the invented probe carrier.

flexible substrate 100

probes immobilized as spots 110

bar codes 120

space between probes 130

Dwg.1/20

TECH UPTX: 20011001

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Probes: The probes comprise polynucleotides comprising single stranded DNA, polypeptides, antibodies, or ligands. The probes are preferably cell surface receptors, oligosaccharides, polysaccharides or lipids. The probes are arranged as a linear configuration of spots, or stripes which are at an angle to the long axis of the substrate. In (III) and M2 - M5 the probes are poly- or oligonucleotides, proteins, polypeptides, oligo- or polysaccharides, antibodies, cell receptors, ligands, lipids, and/or cells, and in (III) the probe binds to a target on them. The target molecules in M2 - M5 are poly- or oligonucleotides, proteins, polypeptides, oligo- or polysaccharides, antibodies, cell receptors, ligands, lipids, and/or cells. The polynucleotides are genes or their fragments, exons, introns, mRNA, tRNA, rRNA, ribozymes, cDNA, recombinant or branched polynucleotides, plasmids, vectors, isolated DNA or RNA, nucleic acid probes or primers.

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Apparatus: (I) further comprises two markers conveying information about two respective sets of probes. The substrate and probes in (II) are enclosed in a container. Both markers are magnetic or optical, or one is magnetic and the other optical. Optical markers are optical bar codes or fluorescent. (I) and (II) are configured as probe-carrying tape or fiber, where the substrate comprises a flexible tape or fiber substrate with a thickness of

at most 500, preferably at most 20, microm, and a surface, and where the probes are immobilized on discrete areas of a probe-containing substrate surface, where each area contains one probe. (I) and (II) comprise a linear 1D probe arrangement which is immobilized on the substrate surface and arranged in single-file at a linear density more than 50, preferably more than 500, probes/cm. (I) and (II) further comprise a layer on the substrate surface where the different probes are immobilized on the surface of the layer, so that the ratio of the length to the width of the probe-carrying portion is more than 5:1. The layer comprises silica. (I) and (II) further comprise another layer between the first layer and the substrate, which comprises a metallic magnetizable material. The substrate comprises a silica glass, a plastic, polymeric, preferably polyimide or polytetrafluoroethylene (PTFE), or metallic magnetizable material, and an optical fiber. Each discrete area has a length at most 1000, preferably less than 20, microm. The ratio of the length to the width of the substrate in M1 and (I) and (II) is more than 5:1, and in (I) and (II) preferably 100 000:1, and M1 100:1. The substrate is wound as a flat spiral and the apparatus comprises two spools. The spiral center is attached to one spool and the outermost end of the substrate extends from the spiral and attaches to the second spool. The apparatus further comprises a flat backing to which the substrate is attached, and one or more drums to which the substrates are wound and attached. The probe carrier in (III) is a flat spiral and comprises a flexible tape or thread substrate carrying a 2D or 1D respectively probe array. A cross-section of the thread substrate has a D shape and the probes are mounted within a notch of the thread surface to protect the probes from friction. The carrier in (I), (II) and (III)comprises one or more probe-carrying sections interspersed with non-carrying sections. (III) further comprises an elongated support member distal to the carrier surface, coiled flexible carriers and elongated support members where each carrier is coiled around a support member, where the carrier surfaces are distal from the members which are attached to a planar support. The support member has a diameter less than 10, or between 10 and 150, mm. (III) also comprises a planar disc support member with an axis with the carrier coiled around it and the carrier surface distal to it, where the probes are circumaxially distributed. The support member has a spiral groove about an axis in a surface of the member through which the carrier is coupled to the member. The member has a diameter 10 - 100 mm and carries at most 1 000 000 probes. The carrier in (III) and M4 is attached to the member by a permanent adhesive, preferably an epoxy cement. The member comprises a magnetic material, preferably at least one magnetic bead, and the carrier is attached between the magnetic materials of the carrier and the member. The carrier is removably coiled on the member. The member has a conductive coating or is metallic. The carrier has a notch on its surface distal to where the carrier contacts the member and the probes are mounted in the notch. The member is in a cassette. The carrier (III) and in M2 - M5 comprises silica, glass, optical fibers, metals, magnetizable metals, plastics, or polymers, preferably polyimide or polytetrafluoroethylene (PTFE). The probe in (III) and M2 - M5 is immobilized on the surface of the carrier by ink jet, silk or offset printing, photolithography, stamping, mechanical application with micropipettes using an x-y stage or a rastering technique, and at least one marker carrying information about the adjacent probe and is positioned on the carrier next to one or more probes. The marker is an optical, space, fluorescent, chemiluminescent, or magnetic marker or a bar codes.
Preferred Method: The probes in M1a are placed on the substrate by spotting in dots or painting in strips, each comprising one probe or in M1 by using tubing containing probes from reservoirs, where a difference in pressure between the reservoir and the tubing, and a voltage between the reservoir and the substrate are applied. Reservoirs comprise wells in microtiter plates and the probes are covalently or non-covalently immobilized on the substrate. Depositing probes on the substrate comprises: moving a single file row of probe-depositing heads, preferably

printing jets and the substrate at the same or different speeds so that the substrate intersects the heads, where the heads comprise a probe-containing liquid reservoir and a thin flexible hydrophilic silica fiber coated with a metal or nylon, and depositing a probe from a head onto the substrate when the head intersects the substrate, where the head brushes the probes onto the substrate and a voltage is applied between the metal and the substrate. The heads are preferably printing jets comprising a pinhole in the reservoir, a piezo ring attached to the reservoir wall, and a voltage source, and which deposit a strip of probe onto the substrate, or a diaphragm at the top of the reservoir and a piezo film coated on the diaphragm. The heads comprise a voltage source and a resistor wire. Probe transfer comprises activating an ultrasound transducer outside the reservoir; illuminating a light absorption patch inside the reservoir with a laser outside the reservoir; or activating a voltage source connected to conductive material on the reservoir walls and to conductive material on the substrate. Depositing the probe on the substrate comprises moving rows of reservoirs comprising a probe and of brushes comprising a flexible strand, so that the brushes intersect the reservoirs and where each brush contacts probe and transfers it to the brush, and moving a substrate positioned so that each brush deposits its probe onto the substrate. The row of brushes is preferably a loop. The brushes are preferably washed after depositing the probes and before returning to the reservoirs. The probes comprise metal, and the method further comprises intermittently charging each brush so that the probe is attracted to the brush when being transferred to the brush, and is repelled when it is deposited. The strip of probe is deposited. Painting the probes in strips comprises dipping fibers into a set of wells, each well containing one probe, where the fibers and set of wells are arranged in two matrices so that the fibers are aligned with the wells, and moving the fibers across a section of the substrate, where each fiber deposits a separate strip of probe across the substrate leaving spaces between the strips. This last method also comprises washing the fibers and repeating the dipping with a second matrix of wells and moving as before. The substrate is made up of several parallel fibers, or is a tape which is separated along its axis after the probes are deposited. The probes are covalently linked to the substrate, and the method further comprises placing 2 probe markers on the substrate. The carrier in M2 resides on an elongated support member to form a carrier pin or rod, where the probe is contacted with a hybridization fluid in a chamber, by immersion in the fluid. The probes are immobilized on several wound flexible elongated carriers as above, where the pins or rods are attached to an adaptor plate to form a matrix with a spatial pitch and a pattern corresponding to microtiter plate wells. The carrier in M3 resides on a planar disc support member and the probe is contacted with a hybridization fluid in a chamber by immersion in the fluid. The wound flexible elongated carrier in M4 forms a flat spiral on an elongated support member to form a flat spool, and probe contacting comprises unspooling the carrier and moving it through the hybridization fluid by drawing the carrier through a slot containing the fluid and comprising a capillary slightly larger than the carrier. The probes are immobilized on several wound flexible elongated carriers, each forming a flat spiral on an individual elongated support member to form several carriers. The probe carrier in M5 is contained in a cassette. M2 - M5 further comprise improving hybridization efficiency by imparting rotational or translational motion to the carrier, using a mechanical adaptor or a magnetic drive, or by applying an alternating current oscillating voltage to the hybridization fluid between the carrier or support member, where the member is contacting the carrier and a wall of the hybridization chamber. A conductive coating on the member is also provided. The probe carrier in M2 - M5 is thread-shaped or a tape and has a notch on the surface distal to the contact point of the member and the carrier, where the probes are mounted in the notch.

L49 ANSWER 55 OF 97 WPIX (C) 2002 THOMSON DERWENT

AN 2001-506375 [56] WPIX
DNN N2001-375712 DNC C2001-152676
TI Detecting complementary nucleic acid fragment with DNA microarray by superposing array with hybridized sample, and fluorescent sheet through spacer having pores corresponding to sample bound positions on the array.
DC B04 D16 **J04 S03**
IN HOSOI, Y; NERIISHI, K; OGURA, N; UMEMOTO, C
PA (FUJF) FUJI PHOTO FILM CO LTD; (HOSO-I) HOSOI Y; (NERI-I) NERIISHI K; (OGUR-I) OGURA N; (UMEM-I) UMEMOTO C
CYC 2
PI JP 2001183372 A 20010706 (200156)* 9p <--
US 2001026917 A1 20011004 (200161) <--
ADT JP 2001183372 A JP 1999-372977 19991228; US 2001026917 A1 US 2000-749410 20001228
PRAI **JP 1999-372977 19991228**
AN 2001-506375 [56] WPIX
AB JP2001183372 A UPAB: 20011001

NOVELTY - Detecting complementary nucleic acid fragments, comprising superposing DNA microarray (I) after hybridization of sample nucleic acid fragment (S) and fluorescent (F) material sheet (II) through spacer having holes in positions corresponding to (S) bound positions of (I), and detecting position of bound (S), is new.

DETAILED DESCRIPTION - Detecting complementary nucleic acid fragment using DNA microarray (I) (11) which comprises several kinds of multiple single stranded (ss) nucleic acid fragment fixed to a supporting unit such that the same kind of multiple ss-nucleic acid fragments are fixed at points different from the different kinds of multiple ss-nucleic acid fragments. The detection method involves:

(a) contacting the sample ss-nucleic acid fragment labeled by radioactive substance, in liquid phase, with (I) so that the sample ss-nucleic acid fragment binds with its complementary sequence ss-nucleic acid fragment on (I) by hybridization;

(b) removing unbound sample ss-nucleic acid fragment from (I);

(c) superposing (I) after hybridization and a storage property-fluorescent material sheet (II) (13), positioning through a spacer (12) having pores (16) in the positions corresponding to the positions of (I) which comprise the bound sample ss-nucleic acid fragment, and where the fluorescent material sheet can accumulate radiation emitted from radioactive label of the sample ss-nucleic acid fragment fixed to (I);

(d) irradiating light on (II) which accumulates the radiation and exhibits a fluorescence phenomenon;

(e) condensing the longer wavelength light emitted by (II) and converting it into electrical signal by photoelectric conversion; and

(f) detecting the position of bonded ss-nucleic acid fragment by processing this electrical signal.

INDEPENDENT CLAIMS are also included for the following:

(1) a detection kit for detecting complementary nucleic acid fragments, the kit comprises (I) fixed to a support body (14) and (II) and the position of the complementary nucleic acid fragment is detected through a spacer which has penetrating pores in positions corresponding to the fixed sample single stranded nucleic acid fragment;

(2) a laminate for detecting complementary nucleic acid fragment which comprises (I) aligned with (II) through a spacer; and

(3) storage property fluorescent material sheet (II) for detecting complementary nucleic acid fragment present on support body (17), is laminated with a spacer having pores at corresponding positions of sample ss-nucleic acid fragments fixed to DNA microarray.

USE - For detecting complementary nucleic acid fragments using DNA microarray and autoradiography, for research purposes, in gene analysis, and in medical fields.

ADVANTAGE - The image formed by radiation has a high resolving degree and sharpness. Accurate gene analysis can be performed in a short time

using the DNA microarray.
DESCRIPTION OF DRAWING(S) - The drawing shows a DNA microarray used in autoradiography purposes for detecting complementary nucleic acid fragments.
DNA microarray 11
Spacer 12
Storage property fluorescent material sheet 13
Support body of DNA microarray 14
Pore 16
Support body of storage property fluorescent material sheet 17.
Dwg.1/3

TECH UPTX: 20011001
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Spacer: The spacer on (II) consists of a material which is impermeable to radiation.

L49 ANSWER 56 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-497068 [54] WPIX
DNN N2001-368318 DNC C2001-149333
TI Collagen-like protein CLAC in brain amyloids, its precursor CLAC-P and their encoded genes, useful in diagnosis, treatment and prevention of Alzheimer's disease by inhibiting amyloid protein accumulation-promoting mechanism.
DC B04 D16 **S03**
IN HASHIMOTO, T; IWATSUBO, T; NAGAI, Y
PA (BFRE-N) BF RES INST INC; (IWAT-I) IWATSUBO T
CYC 30
PI WO 2001058943 A1 20010816 (200154)* JA 86p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU CA CN HU IN JP KR NO NZ RU US
AU 2001032275 A 20010820 (200175)
ADT WO 2001058943 A1 WO 2001-JP1014 20010214; AU 2001032275 A AU 2001-32275 20010214
FDT AU 2001032275 A Based on WO 200158943
PRAI **WO 2000-JP788 20000214**
AN 2001-497068 [54] WPIX
AB WO 200158943 A UPAB: 20010924
NOVELTY - A CLAC DNA containing nucleotides from 868-2493 of a defined base sequence (I) given in the specification, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a CLAC containing amino acids from 113-654 of a defined amino acid sequence (II) given in the specification;
(2) a DNA encoding a protein based on (II) but with some amino acids inserted, deleted or substituted, and has the following characteristics of (a) and (b):
(a) accumulating in the aged plaque amyloid component of patients with Alzheimer's disease; and
(b) having a function of A beta aggregation;
(3) a DNA hybridizable with the above DNA (I) under stringent conditions that encodes a protein with the above characteristics of (a) and (b);
(4) a protein encoded any of the DNAs;
(5) a CLAC-P containing an amino acid sequence of (II);
(6) a DNA encoding a protein based on the above CLAC-P but with some amino acids inserted, deleted or substituted, and functions as A beta receptor on cells surface;
(7) a DNA hybridizable with the CLAC-P DNA under stringent conditions and functioning as A beta receptor on cells surface;
(8) a protein encoded by any of the DNAs;
(9) expression vectors containing the DNAs;
(10) transformants which are transformed with the vectors;
(11) a method for producing a recombinant protein by culturing the transformant to express the vector to give a product;

(12) a transformant with an Accession Number of FERM BP-7438;
(13) a CLAC-P gene which is contained in the transformant with an Accession Number of FERM BP-7438;
(14) a method for producing a recombinant protein by culturing the transformant FERM BP-7438 to express the vector to give a product;
(15) an antibody specifically for the protein;
(16) a method for screening inhibitors of CLAC activity by using the protein;
(17) CLAC inhibitors thus screened;
(18) a method for detecting CLAC by using the antibody;
(19) a method for treating, delaying the progress of or preventing Alzheimer's disease by using the specified antibody or CLAC inhibitor;
(20) a method for purifying CLAC by using monoclonal antibody 9D2;
(21) an antibody that can specifically bind with the CLAC-P protein;
(22) a method for screening inhibitors of CLAC-P activity by using the protein;
(23) CLAC-P inhibitors thus screened;
(24) a method for detecting CLAC-P by using the antibody;
(25) a method for treating, delaying the progress of or preventing Alzheimer's disease by using the specified antibody or CLAC-P inhibitor;
(26) a method for purifying CLAC-P by using monoclonal antibody 9D2;
(27) a kit for diagnosing Alzheimer's disease comprising a detectably labeled monoclonal antibody 9D2; and
(28) a transgenic animal which has been artificially transfected with any of the DNAs, or is defective of the chromosome.
ACTIVITY - Anti-Alzheimer's.
MECHANISM OF ACTION - Vaccine.
USE - The proteins and encoded genes are useful in diagnosis, treatment and prevention of Alzheimer's disease by inhibiting amyloid protein accumulation-promoting mechanism and cell damage.
Dwg.0/4

TECH UPTX: 20010924
TECHNOLOGY FOCUS - BIOTECHNOLOGY - The protein is particularly based on the defined sequence (II), given in the specification, in which some amino acids in the amino acids from 141-146 or 589-597 are deleted or substituted.

TECHNOLOGY FOCUS - BIOLOGY - The antibody is monoclonal antibody 9D2.

L49 ANSWER 57 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-465363 [50] WPIX
CR 2001-442253 [47]; 2001-442255 [47]; 2001-451890 [48]; 2001-451908 [48]; 2001-451909 [48]; 2001-451912 [48]; 2001-451938 [48]; 2001-451939 [48]; 2001-457603 [49]; 2001-457740 [49]; 2001-465571 [50]; 2001-465578 [50]; 2001-465705 [50]; 2001-476114 [50]; 2001-476164 [50]; 2001-476197 [50]; 2001-476198 [50]; 2001-476199 [50]; 2001-476282 [51]; 2001-476283 [51]; 2001-483140 [52]; 2001-483233 [50]; 2001-488707 [53]; 2001-488788 [50]; 2001-488875 [53]; 2001-488895 [52]; 2001-496929 [52]; 2001-496930 [52]; 2001-496931 [52]; 2001-496932 [52]; 2001-514838 [56]; 2001-522358 [52]; 2001-565565 [60]; 2001-582152 [58]; 2001-582153 [58]; 2001-589862 [58]; 2001-589934 [60]; 2001-607699 [69]; 2001-611724 [70]; 2001-611725 [70]; 2001-626375 [68]; 2001-626426 [68]; 2001-626432 [68]; 2001-626527 [70]; 2001-639362 [67]; 2002-010428 [50]; 2002-025688 [52]; 2002-062370 [05]; 2002-280918 [22]
DNC C2001-140501
TI New phospholipase-like polypeptides and polynucleotides useful for treating or preventing e.g. autoimmune diseases, neurological disorders or conditions, cardiac dysfunctions or neurolopathies.
DC B04 D16
IN ARTERBURN, M C; BOYLE, B J; DRMANAC, R T; KUO, C; LIU, C; TANG, Y T
PA (HYSE-N) HYSEQ INC
CYC 94
PI WO 2001053326 A1 20010726 (200150)* EN 201p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001025918 A 20010731 (200171)

ADT WO 2001053326 A1 WO 2000-US34977 20001222; AU 2001025918 A AU 2001-25918 20001222

FDT AU 2001025918 A Based on WO 200153326

PRAI **US 2000-691291 20001017; US 1999-471275 19991223 ; US 2000-488725 20000121; US 2000-496914 20000203; US 2000-552317 20000425; US 2000-560875 20000427**

AN 2001-465363 [50] WPIX

CR 2001-442253 [47]; 2001-442255 [47]; 2001-451890 [48]; 2001-451908 [48]; 2001-451909 [48]; 2001-451912 [48]; 2001-451938 [48]; 2001-451939 [48]; 2001-457603 [49]; 2001-457740 [49]; 2001-465571 [50]; 2001-465578 [50]; 2001-465705 [50]; 2001-476114 [50]; 2001-476164 [50]; 2001-476197 [50]; 2001-476198 [50]; 2001-476199 [50]; 2001-476282 [51]; 2001-476283 [51]; 2001-483140 [52]; 2001-483233 [50]; 2001-488707 [53]; 2001-488788 [50]; 2001-488875 [53]; 2001-488895 [52]; 2001-496929 [52]; 2001-496930 [52]; 2001-496931 [52]; 2001-496932 [52]; 2001-514838 [56]; 2001-522358 [52]; 2001-565565 [60]; 2001-582152 [58]; 2001-582153 [58]; 2001-589862 [58]; 2001-589934 [60]; 2001-607699 [69]; 2001-611724 [70]; 2001-611725 [70]; 2001-626375 [68]; 2001-626426 [68]; 2001-626432 [68]; 2001-626527 [70]; 2001-639362 [67]; 2002-010428 [50]; 2002-025688 [52]; 2002-062370 [05]; 2002-280918 [22]

AB WO 200153326 A UPAB: 20020521

NOVELTY - An isolated polynucleotide (I) comprising a fully defined sequence of 365 (P1), 398 (P2), 555 (P3), 403 (P4), 4875 (P5), 4820 (P6), 4875 (P7), 2133 (P8) or 4803 (P9) base pair (bp) given in the specification, the translated protein coding portions, the mature protein coding portions, the extracellular portion, or the active domains, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide which:

(a) encodes a polypeptide with biological activity;

(b) hybridizes to the complement (I) under stringent hybridization conditions;

(c) has greater than 90% sequence identity with P1, P2, P3, P4, P5, P6, P7, P8, P9 or a defined 2133 bp sequence (P10); or

(d) comprises the complement of (I);

(2) an expression vector comprising (I);

(3) a host cell genetically engineered to express (I);

(4) an isolated polypeptide (II) comprising an amino acid sequence which is at least 90% identical to a fully defined sequence of 1624 (S1), 710 (S2), 1600 (S3), 14 (S4), 23 (S5), 687 (S6), 180 (S7), 134 (S8), 107 (S9), 128 (S10), 128 (S11), 130 (S12), 163 (S13), 112 (S14), or 120 (S15) amino acids given in the specification, the translated protein coding portion, the mature protein coding portion, the extracellular portion, or the active domain of these polypeptides;

(5) a composition comprising (II) and a carrier;

(6) a polypeptide, having phospholipase-like activity, comprising at least 10 consecutive amino acids from an amino acid sequence selected from S4, S5, S7-S14, and S15;

(7) polynucleotides encoding the polypeptides;

(8) an antibody specific for (II);

(9) methods for detecting (I) in a sample;

(10) a method for detecting (II) in a sample;

(11) methods for identifying a compound that binds (II);

(12) a method of producing a phospholipase-like polypeptide;

(13) a kit comprising (II);

(14) a nucleic acid array comprising (I) or a unique segment of (I) attached to a surface;

(15) a method of treating a subject in need of enhanced activity or expression of phospholipase-like polypeptide of claim 10 by administering (II), an agonist of (II), or a polynucleotide encoding (II), and a carrier;

(16) a method of treating a subject having a need to inhibit activity or expression (II) by administering an antagonist of (II), a nucleic acid inhibiting the expression of the nucleotide sequence encoding (II), or a polypeptide that competes with the phospholipase-like polypeptide for its ligand, and a carrier.

ACTIVITY - Cerebroprotective; nootropic; cytostatic; immunosuppressive; anti-viral; vulnerary.

MECHANISM OF ACTION - Gene therapy.

USE - The polypeptides and polynucleotides are useful in the prevention and/or treatment of disorders mediated by loss or overexpression of phosholipase-like polypeptide, e.g. rheumatoid arthritis, septic shock, or pancreatitis, as well as for the diagnosis, treatment or prevention of neurological conditions and disorders. The polypeptides and polynucleotides may also be used as nutritional sources or supplements. The polypeptides may also be used to prevent cardiac dysfunction and neuropathology under stress conditions such as cardiac anaphylaxis or seizures, to treat, prevent or ameliorate a medical condition including viral diseases. These polypeptides may further be used in wound healing and tissue repair and replacement, and in healing burns incisions and ulcers. The polynucleotides may be used to express recombinant protein for analysis, characterization or therapeutic use, as molecular weight markers on gels, as chromosome markers or tags to identify chromosomes or to map related gene positions, to compare with endogenous DNA sequences in patients to identify potential genetic disorder, as probes to hybridize and thus discover novel, related DNA sequences, as source of information to derive polymerase chain reaction (PCR) primers for genetic fingerprinting, to raise anti-protein antibodies, and as an antigen to raise anti-DNA antibodies or elicit immune response. Compositions comprising the polypeptides or polynucleotides are useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies e.g. Alzheimer's or Parkinson's disease, as well as mechanical and traumatic disorders; for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury and conditions resulting from systemic cytokine damage; for promoting tissue differentiation; treating autoimmune diseases, e.g. multiple sclerosis, systemic lupus erythematosus.

Dwg.0/6

TECH UPTX: 20010905

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Polynucleotide: (I) is a DNA. (I) when comprised in the host cell is in operative association with a regulatory sequence that controls expression of the polynucleotide in the host cell.

Preferred Polypeptide: The polypeptide comprises at least 5 consecutive amino acids from the polypeptide sequences selected S4, S5, S7-S14, and S15.

Preferred Method: The method of detecting (I) in a sample comprises contacting the sample with a compound that binds to and forms a complex with (I), and detecting the presence of the complex, indicating the presence of the (I). Alternatively, the method comprises contacting the sample under stringent hybridization conditions with nucleic acid primers that anneal to (I), amplifying a product comprising at least a portion (I), and detecting the product and (I) in the sample. (I) comprises an RNA molecule and the method further comprises reverse transcribing an annealed RNA molecule into a cDNA polynucleotide. Identifying a compound that binds to (II), comprises contacting the compound with (II) under conditions allowing the formation of a polypeptide/compound complex, and detecting

the presence of the complex, which indicates that compound that binds (II). Alternatively, the method comprises contacting the compound with (II) in a cell, to form a polypeptide/compound complex, which drives the expression of a reporter gene sequence in the cell, and detecting the complex by detecting reporter gene sequence expression, indicating that the compound binds to (II). Producing a phospholipase-like polypeptide comprises culturing the host cell under conditions for the expression of the polypeptide, and isolating the polypeptide from the cell culture or cells.
Preferred Array: The array detects full-matches to (I).

L49 ANSWER 58 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-343808 [36] WPIX
DNC C2001-106493
TI Microarray for simultaneously detecting large numbers of proteins where some are in trace amounts, comprises immobilized oligonucleotides complementary to sequence tags.
DC B04 D16
IN ANDERSON, N L
PA (LARG-N) LARGE SCALE PROTEOMICS CORP
CYC 93
PI WO 2001036585 A1 20010525 (200136)* EN 34p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001019210 A 20010530 (200152) <--
ADT WO 2001036585 A1 WO 2000-US31516 20001117; AU 2001019210 A AU 2001-19210 20001117
FDT AU 2001019210 A Based on WO 200136585
PRAI **US 1999-166266P 19991118**
AN 2001-343808 [36] WPIX
AB WO 200136585 A UPAB: 20010628
NOVELTY - A microarray (I) having immobilized oligonucleotides complementary to sequence tags, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a recombinant microorganism (II) capable of expressing a specific receptor in its surface and containing a unique nucleic acid sequence tag;
(2) different recombinant (II), each containing a different specific receptor and nucleic acid sequence tag;
(3) a nucleic acid labeled receptor (III) comprising a specific binding receptor and a nucleic acid containing at least 13 nucleotides which is physically or chemically bound to the receptor;
(4) a plurality of (III) where each receptor specifically binds to a different ligand and is labeled with a nucleic acid having a different sequence;
(5) a microarray (IV) comprising a solid phase containing cells in a definable location, nucleic acids immobilized on the solid phase, where each cell contains all of the nucleic acids of a particular sequence, and a nucleic acid sequence specifically hybridized to the nucleic acid;
(6) determining the presence of a ligand in a mixture sample of ligands comprising contacting at least one of (II) or the nucleic acid labeled receptor for binding, and separating bound and unbound and detecting at least one sequence tag;
(7) a solid support having immobilized ligands and receptors bound to the ligands;
(8) a solid support (V) having bound different recombinant microorganisms, each capable of expressing a specific receptor on its surface and each having a heterologous gene encoding the receptor; and
(9) fractionating (VI) a mixture of recombinant microorganisms, each

capable of expressing a different specific receptor on its surface, comprising contacting the mixture with a solid support and allowing at least part of the mixture to bind, and removing unbound microorganisms.

USE - The microarray is useful for simultaneously determining the presence of a ligand in a mixture of different ligands (claimed). The microarray is especially useful for detecting large numbers of different proteins in a mixture, even where certain proteins occur in trace amounts relative to the other proteins.

ADVANTAGE - The method is the only to detect large numbers of different proteins where certain proteins occur in trace amounts relative to other proteins.

Dwg.0/6

TECH UPTX: 20010628

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Array: The sequence tags in (I) have a random sequence.

The tags in (IV) are hybridized to the cells. The sequence tag is part of a nucleic acid containing at least part of an antibody gene, or part of a microorganism or cellular gene.

Preferred Microorganism: The sequence tag is part of a nucleic acid containing at least part of an antibody gene, or part of a microorganism or cellular gene.

Preferred Method: Quantitative measuring is by determining the quantity of sequence tag from bound receptors. Simultaneous detection by detecting corresponding different tags can be done. The concentration of one ligand being detected is at least ten fold greater than another ligand in the sample. The nucleic acid containing the sequence tag is preferably labeled. Detection is by specific hybridization to complementary nucleic acids which are physically separated or separable from each other. The commentary nucleic acids are located in an array on a solid phase.

The nucleic acids containing the sequence tag is amplified. The ligands are proteins and the receptors expressed form an antibody-derived gene. The receptor may be on the surface of a virus.

A known quantity of a control ligand my be administered to determine ligands levels relative to controls.

In (VI) bound microorganisms are eluted from the support. The microorganisms are bound by the receptor to ligands on the support, and the method further comprises initially immobilizing ligands on the support. The receptor may bind to the ligands before immobilizing the ligands on the support.

Preferred Support: The support is bound to a ligand which is bound to the receptor on the microorganism.

L49 ANSWER 59 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-158471 [16] WPIX
CR 1998-168403 [15]; 1998-427022 [36]; 1998-541762 [46]
DNN N2001-115427 DNC C2001-046958
TI Detection of oligonucleotides such as DNA and RNA useful e.g. to identify bacteria and viruses in clinical and environmental samples and for DNA mapping uses surface-enhanced Raman scattering label detection.
DC B04 D16 **S03**
IN VO-DINH, T
PA (UTBA-N) UT-BATTELLE LLC
CYC 1
PI US 6174677 B1 20010116 (200116)* 37p <--
ADT US 6174677 B1 CIP of US 1995-543212 19951013, US 1998-161897 19980928
FDT US 6174677 B1 CIP of US 5814516
PRAI **US 1998-161897 19980928; US 1995-543212 19951013**
AN 2001-158471 [16] WPIX
CR 1998-168403 [15]; 1998-427022 [36]; 1998-541762 [46]
AB US 6174677 B UPAB: 20010323

NOVELTY - Oligonucleotides such as DNA are detected and identified using a non-radioactive method based on surface-enhanced Raman scattering (SERS) label detection, in which a gene probe immobilized on a nonSER-active

support means is used to hybridize with, detect and identify a SER-labeled target oligonucleotide.

DETAILED DESCRIPTION - The method comprises:

(a) preparing a solution of gene probe oligonucleotide strands complementary to a target oligonucleotide strand;

(b) incubating the gene probe strands with a support means to immobilize them on the support;

(c) synthesizing at least one SER-labeled oligonucleotide strand of unknown sequence taken from a sample suspected of containing a target oligonucleotide, the strand having at least one SER label unique for the target oligonucleotide sequence;

(d) preparing a SER-labeled oligonucleotide solution comprising at least one strand as in (c);

(e) incubating the support and solution in conditions allowing hybridization of the gene probe strands and the SER-labeled oligonucleotide strands to produce SER-labeled hybridized target oligonucleotide material;

(f) removing non-hybridizing SER-labeled oligonucleotide strands;

(g) activating the support with a SER activating means; and

(h) analyzing the SER-activated support having SER-labeled hybridized target oligonucleotide material.

INDEPENDENT CLAIMS are also included for modified methods as follows:

(i) steps (a)-(d) comprise immobilizing the oligonucleotide strands onto the support and SER-labeling the gene probe;

(ii) steps (c)-(e) comprise preparing a solution comprising oligonucleotide strands from a sample and at least one SER label, and incubating the solution with immobilized gene probe strands so that the SER label is intercalated between hybridized oligonucleotides;

(iii) as in (ii) in which the gene probe is not SER-labeled, but incubated with the support in a solution also comprising at least one SER label; and

(iv) methods in which the support is SERS activated during hybridization, comprising incubating the support with a solution comprising a SERS activating means and either oligonucleotide strands from a sample and SER-labeled gene probe strands or SER-labeled oligonucleotide strands and gene probe strands, simultaneously SERS activating the support with a SERS activating means and analyzing the support.

USE - The method is useful for detection and identification of oligonucleotides such as DNA, RNA or peptide nucleic acids (claimed). It can be used to identify microorganisms e.g. Salmonella bacteria during food processing, Legionella bacteria, (the causative agent for pneumonia) in water samples, DNA and RNA viruses linked with cancer (e.g. Papovavirus) etc. It is also useful to detect genetic diseases or susceptibility and DNA polymorphisms, in drug discovery and for DNA mapping.

ADVANTAGE - Molecular probes having a SERS label provide an excellent combination of detection sensitivity and spectral selectivity, important for many bioassays.

Dwg.0/20

TECH UPTX: 20010323

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The support means may be e.g. a substrate or membrane suitable for hybridization, a blotting material, polymer-based nanosphere etc. or have a surface comprising cellulose, silica gel or polystyrene. The SERS activating means preferably comprises e.g. coating the support with metal coated magnetic nanobeads, inducing an electrochemical reaction to roughen the surface of the support etc. The SER-activated support means is preferably disposed on a fiberoptic probe or waveguide enabling generation and transmission of Raman optical signals (especially multiple SER-activated support means disposed on an array of optical fibers or on a waveguide, enabling multiple assays of uniquely labeled hybridized oligonucleotides); details are given in the specification.

L49 ANSWER 60 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-122094 [13] WPIX
CR 1999-312595 [26]
DNN N2001-089586 DNC C2001-035335
TI Biochemical sensor element structure useful for nucleic acid separation, purification, isolation and synthesis, comprises solid **substrate** , and monolayer of alkylsilane groups bound to its surface.
DC A96 B04 D16 P42
IN MCGOVERN, M; THOMPSON, M
PA (MCGO-I) MCGOVERN M; (THOM-I) THOMPSON M
CYC 1
PI US 6159695 A 20001212 (200113)* 21p <--
ADT US 6159695 A CIP of US 1997-951448 19971016, US 1999-301287 19990428
PRAI **US 1999-301287 19990428; US 1997-951448 19971016**
AN 2001-122094 [13] WPIX
CR 1999-312595 [26]
AB US 6159695 A UPAB: 20010307
NOVELTY - A biochemical sensor element structure (I) comprises a solid **substrate** (II), a surface (III) on (II) and a monolayer of alkylsilane groups chemically bound to (II), where the alkylsilane groups are cross-linked to one another, and has distal reactive chemical groups, and the alkylsilane groups are bonded to (III) at a density of at least 14 picomoles per square centimeter of area of (II).
DETAILED DESCRIPTION - In (I) the distal chemical reactive groups comprises protected thiol groups of general formula (F1).
-S-CO-CX3 (F1).
Where:
X = a halo adapted for deprotection and chemical bonding directly or indirectly to a bio-molecule.
USE - (I) is useful in nucleic acid separation, purification, isolation, synthesis, amplification, and in diagnostic or detection applications.
ADVANTAGE - (I) has a very high density of bio-molecules immobilized on it, and is disposed and oriented for chemical and biochemical reaction of high sensitivity.
Dwg.0/5
TECH UPTX: 20010307
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Structure: (I) comprises at least two different alkylsilane groups bound to the surface, the first alkylsilane group being terminated at its distal end by the functional group, and a second alkyl silane group being a diluent silane of shorter alkyl group chain length than the first alkylsilane group and being chemically inert at its distal end. The alkylsilane groups have 2-20 carbon atoms, preferably 8-18 carbon atoms in the alkyl chain. The alkylsilane groups are bonded to (III) through Si-O-groups, and are cross-linked to one another through the same Si-atoms. The alkylsilane group has a linear alkyl chain of 11 methylene groups and is derived from 1-(thiofluorocetato)-11-trichlorosilyl) undecane. The X in the general formula -S-CO-CX3, is preferably fluorine. (II) is silicon, metal, silicon oxide or metal oxide.

L49 ANSWER 61 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-082700 [10] WPIX
DNC C2001-024075
TI Sample preparation for DNA analysis comprises amplifying two or more different DNA fragments by polymerase chain reaction using combinations of specific primers immobilized on different supports.
DC B04 D16
IN KAMBARA, H
PA (HITA) HITACHI LTD
CYC 27
PI EP 1061136 A2 20001220 (200110)* EN 27p <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

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        RO SE SI
     JP 2000342258 A  20001212 (200113)       15p <--
     US 2001018412 A1 20010830 (200151)           <--
     US 2001019824 A1 20010906 (200154)           <--
ADT  EP 1061136 A2 EP 2000-112246 20000607; JP 2000342258 A JP 1999-162038
     19990609; US 2001018412 A1 Cont of US 2000-587613 20000605, US 2001-793681
     20010227; US 2001019824 A1 Cont of US 2000-587613 20000605, US 2001-793098
     20010227
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PRAI **JP 1999-162038 19990609**

AN 2001-082700 [10] WPIX

AB EP 1061136 A UPAB: 20010220

NOVELTY - Sample preparation method for DNA analysis comprises: (a) amplifying two or more different DNA fragments by polymerase chain reaction (PCR) by using combinations of specific primers which have base sequences complementary to the DNA fragments to be amplified, are immobilized on the surfaces of different supports and bind specifically to the DNA fragments, and a free primer present in solution; and (b) separating and recovering the PCR amplification products produced on the surfaces of the supports.

An INDEPENDENT CLAIM is also included for:

(1) a sample preparation apparatus for DNA analysis which comprises a holder having a plurality of through-holes for holding specific primers so as to separate them on the basis of their kinds, the specific primers having base sequences complementary to two or more kinds, respectively, of DNA fragments to be amplified, and the specific primers being capable of binding specifically to the two or more kinds, respectively, of the DNA fragments and a concavity which accommodates a PCR solution containing a common primer capable of hybridizing with the base sequence of an oligonucleotide introduced into the 3'-end of each of the DNA fragments, and the DNA fragments, and receives one edge of the holder, where the PCR amplification of the DNA fragments is carried out by using combinations of each of the specific primers and the common primer, to produce PCR amplification products derived from the DNA fragments of each kind, inside the corresponding hole; and

(2) DNA analysis, which comprises a step of synthesizing complementary strands by hybridizing fragments of DNAs to be inspected, with different primers for synthesis of the complementary strands which have been immobilized on two or more groups of supports so as to correspond to the kinds of the supports, the supports being different in a physical property, and the kinds of the supports being discriminable from one another; and a step of separating and recovering the products of the complementary strand synthesis on the basis of the kinds of the fragments in the samples, by monitoring the difference in the physical property.

USE - For quantitative cDNA analysis, e.g. gene expression profiling.

ADVANTAGE - Multiple DNA fragments can be amplified simultaneously without interference between the different primers.

Dwg.0/14

TECH UPTX: 20010220

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The free primer is a common primer that hybridizes with all of the DNA fragments, or with an oligonucleotide introduced into 3' or 5' end of each of the DNA fragments. The supports are either: (i) fine particles having different specific gravities or sizes; (ii) fibers with the specific primers immobilized near the fiber ends; (iii) fine particles which can be discriminated, preferably on the basis of size, specific gravity, color or degree of magnetization, and are accommodated in a single reaction cell; or (iv) fine particles which are separately held in different compartments inside a single capillary, preferably separated by spacer particles. The supports are beads having different colors, and the synthesis products derived from the DNA fragments in the samples are separated and recovered on the basis of their kinds by optically monitoring the kinds of the beads while allowing the beads to flow. The synthesis products derived from the DNA fragments in the samples are separated and recovered on the basis of

their kinds by monitoring the kinds of the beads on the basis of the specific gravities. The supports are fibers that can be discriminated from one another on the basis of any outer shape, color and dimensions. The immobilized primers are held in different places so as to be separated on the basis of the kinds of the primers, PCR is carried out by hybridizing the fragments of the DNAs to be inspected, with the primers to trap the fragments, and the PCR products are separated and recovered on the basis of the kinds of the fragments of the DNAs to be inspected. The supports are held in a transparent capillary, in regions spatially isolated from one another. The supports are held in holes formed so as to be spatially isolated from one another.
Preferred Apparatus: The fine particles immobilizing the specific primers are held on the inner surface of the capillary. Thin pieces including fibers which have the specific primers immobilized on them are held in the capillary.

L49 ANSWER 62 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-071113 [08] WPIX
DNN N2001-053804 DNC C2001-019915
TI New sensor for detection of DNA or RNA from target organisms, comprising an electrode with attached oligonucleotides which are modified with attached electron donor and acceptor Groups.
DC B04 D16 T01
IN MEGERLE, C A
PA (LOCK) LOCKHEED MARTIN CORP; (MEGE-I) MEGERLE C A
CYC 93
PI WO 2000075792 A2 20001214 (200108)* EN 27p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000054590 A 20001228 (200119) <--
US 6391624 B1 20020521 (200239) <--
ADT WO 2000075792 A2 WO 2000-US15221 20000602; AU 2000054590 A AU 2000-54590 20000602; US 6391624 B1 Provisional US 1999-137597P 19990603, Provisional US 1999-154037P 19990916, US 2000-585549 20000602
FDT AU 2000054590 A Based on WO 200075792
PRAI **US 1999-154037P 19990916; US 1999-137597P 19990603 ; US 2000-585549 20000602**
AN 2001-071113 [08] WPIX
AB WO 200075792 A UPAB: 20010207
NOVELTY - New sensors for the detection of DNA or RNA from target organisms comprise an electrode with attached oligonucleotides (ONs) which are modified with attached electron donor and acceptor groups.
DETAILED DESCRIPTION - A novel improved sensor cell for the detection of the presence of DNA or RNA from a target organism comprises an electrode and different groups of modified ONs attached to the electrode. The ON groups are complementary to groups of target sequences of DNA or RNA in a target biological agent. The modification consisting of the attachment of electron donor and electron acceptor groups on the ribose backbone of the ONs, and the sensor cell may form multiple hybridized pairs with DNA or RNA from a single target biological agent.
INDEPENDENT CLAIMS are also included for the following:
(1) a biosensor assembly for the remote detection of the presence of nucleic acid sequences comprising:
(a) a sensor cell comprising an electrode and different groups of single stranded (ss) modified ONs, each group comprising identical complementary nucleotide sequences (NSs) to characteristic sequence of nucleic acids of a target biological agent (each of the ONs from each of the groups is attached to the electrode and the modification comprises the attachment of at least one redox groups on each of the ONs);

(b) a sample preparation chamber for creating a hybridization solution, the chamber incorporating a cell lysis device to rupture a cell membrane and release DNA into solution and a denaturing device to reduce the DNA into a ss catenate molecules;

(c) flow control elements to introduce the hybridization mixture to the electrode;

(d) an electrochemical detection device to determine if the hybridization mixture has bonded with the modified ONs and provide an output in response to the presence of a hybridized pair;

(e) a processor to analyze the output from the electrochemical detector, and instruct the flow control elements;

(f) a communication device to convey information relating to the existence of hybridized molecules on the surface of the sensor cell; and

(g) a power source for energizing the detection device, the processor, the flow control elements and the communication device;

(2) detecting the presence of low levels of a specific biological agent comprising:

(a) capturing a sample containing unknown DNA or RNA;

(b) releasing the DNA or RNA into a solution;

(c) denaturing the DNA or RNA into ss molecules and thereby creating a hybridization mixture;

(d) introducing the hybridization mixture to a sensor cell containing groups of modified ONs attached to a single electrode (the modification consisting of the attachment of molecules);

(e) application of a current to the sensor cell;

(f) measuring of the conductivity of the hybridization mixture; and

(3) constructing a highly sensitive biological agent detection cell comprising:

(a) selecting unique segments of DNA or RNA from a target biological agent;

(b) synthesizing groups of ONs complementary to the unique segments;

(c) modifying the ON with electron donor and acceptor moieties; and

(d) attaching the modified ONs from the groups to an electrode within the cell.

USE - The sensors can be used for the detection of DNA or RNA from target agents such as human pathogens, prokaryotic organisms or viruses (claimed). They can be used in environmental and battlefield applications and in disease diagnosis, genetic screening and drug development.

ADVANTAGE - The modification of ONs by the attachment of electron donor and acceptor groups can greatly increase the conductivity of hybridized molecules. Providing unique complementary ON groups to a single electrode increases the sensitivity of the probe by both diminishing the steric hindrance effects on the surface of the probe such as crowding and tangling and by providing more potential bonding sites per molecule of the target DNA. These characteristics result in a probe having increased sensitivity and which is particularly effective for the detection of DNA or RNA of target biological agents at very low levels.

DESCRIPTION OF DRAWING(S) - The drawing shows a biological sensor assembly:

Preparation chamber 12
Sensor cell 14
Detection device 16
A central processing unit 18
Output 20
Intake port 22
Power source 68
Outlet port 70
Dwg.1/6

TECH UPTX: 20010207

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Biosensor Assembly: Target DNA is released by the biosensor by employing osmotic pressure to lyse the cell membrane of the target biological agent.

In the presence of a target DNA in the sample, the biosensor provides an

audible signal such as an alarm, an electric signal that can be carried to a remote receiving device, an electronic signal such as a radio signal or an optical signal.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Group: The group attached to the ON groups may be ferrocene.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred moiety: The group attached to the ON groups may also be ruthenium.

L49 ANSWER 63 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-025030 [03] WPIX
DNC C2001-007698
TI High efficiency, high throughput methods for, e.g., identification and elimination of redundancy in nucleic acid populations, using microarrays and a reiterative subtraction protocol.
DC B04 D16
IN CALL, K; CONNOLLY, T; PERRIN, S; CONNELLY, T
PA (AVET) AVENTIS PHARM INC; (CALL-I) CALL K; (CONN-I) CONNELLY T; (PERR-I) PERRIN S
CYC 94
PI WO 2000070098 A1 20001123 (200103)* EN 37p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000051455 A 20001205 (200113) <--
BR 2000011297 A 20020226 (200223) <--
NO 2001005635 A 20020115 (200224) <--
EP 1185699 A1 20020313 (200225) EN <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2002051970 A1 20020502 (200234) <--
ADT WO 2000070098 A1 WO 2000-US13789 20000519; AU 2000051455 A AU 2000-51455 20000519; BR 2000011297 A BR 2000-11297 20000519, WO 2000-US13789 20000519; NO 2001005635 A WO 2000-US13789 20000519, NO 2001-5635 20011119; EP 1185699 A1 EP 2000-936091 20000519, WO 2000-US13789 20000519; US 2002051970 A1 US 1999-314698 19990519
FDT AU 2000051455 A Based on WO 200070098; BR 2000011297 A Based on WO 200070098; EP 1185699 A1 Based on WO 200070098
PRAI **US 1999-314698 19990519**
AN 2001-025030 [03] WPIX
AB WO 200070098 A UPAB: 20010116
NOVELTY - Microarray-based subtractive hybridization methods are used for, e.g., reducing redundancy in samples of nucleic acid molecules (NAMs) or for identifying non-redundant sequences in a population of NAMs.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) reducing redundancy in a sample of NAMs, comprising:
(a) providing a heterogeneous sample of NAMs;
(b) immobilizing the sample of NAMs on a first microarray;
(c) hybridizing, to the sample, one or more labeled probes corresponding to sequences which are known to be, or suspected to be, present in said sample of NAMs;
(d) identifying at least one immobilized NAM that hybridizes weakly or does not hybridize to the labeled probes;
(e) providing a probe which specifically recognizes the NAM identified in (d); and
(f) optionally repeating steps (b)-(d) or (b)-(e) using a labeled probe which includes the probe of step (e), thus reducing redundancy in the sample of nucleic acid molecules;

(2) identifying a non-redundant sequence in a population of NAMs, comprising:

(a) providing a heterogeneous sample of NAMs;

(b) immobilizing the sample of NAMs on a microarray;

(c) hybridizing one or more labeled probes corresponding to previously arrayed or sequenced NAMs;

(d) identifying at least one immobilized NAM that hybridizes weakly or does not hybridize to the labeled probes; and

(e) sequencing the NAM identified in step (d), thus identifying a sequence which is present in low copy number in the population;

(3) identifying a plurality of non-redundant sequences in a population of NAMs, comprising:

(a) providing a heterogeneous sample of NAMs;

(b) immobilizing the sample of NAMs on a microarray;

(c) hybridizing one or more labeled probes to the sample;

(d) identifying at least one immobilized NAM that hybridizes weakly or does not hybridize to the labeled probes; and

(e) repeating steps (a)-(d) or (b)-(d), thus identifying a plurality of non-redundant NAMs in the population;

(4) identifying multiple non-redundant sequences in a random sample of NAMs, comprising:

(a) amplifying a heterogeneous sample of NAMs;

(b) immobilizing the sample of NAMs on a solid surface in a microarray format;

(c) hybridizing labeled probes from a DNA source to the immobilized NAMs;

(d) identifying at least one immobilized NAM that hybridizes weakly or does not hybridize to the labeled probe;

(e) determining the sequence of the NAM identified in (d); and

(f) reiterating steps (b)-(e) or (c)-(e), thus identifying multiple non-redundant sequences in the sample;

(5) identifying multiple NAMs corresponding to a whole genome or regions of interest, comprising:

(a) amplifying a heterogeneous sample of genomic NAMs from a whole genome or subregion of interest;

(b) immobilizing the amplified NAMs on a solid surface in a microarray format;

(c) hybridizing labeled probes from a DNA source to the immobilized NAMs;

(d) detecting DNA NAMs which hybridize to the labeled probe;

(e) determining the sequence of the NAM identified in (d); and (f) reiterating steps (b)-(e) or (c)-(e), thus identifying multiple NAMs corresponding to a whole genome or region of interest;

(6) identifying nucleic acid sequences that are present in different amounts in a first population and a second population of NAMs, comprising:

(a) amplifying a heterogeneous sample of NAMs;

(b) immobilizing the amplified NAMs on a solid surface in a microarray format;

(c) hybridizing labeled probes from a first population of NAMs and labeled probes from a second population of NAMs to the immobilized NAMs;

(d) detecting NAMs which hybridize to a labeled probe from the first source or the second source; and

(e) determining the sequence of the NAM identified in (d);

(7) discovering a nucleic acid sequence related to a known nucleic acid sequence, comprising:

(a) amplifying a heterogeneous sample of NAMs;

(b) immobilizing the amplified NAMs on a solid surface in a microarray format;

(c) hybridizing labeled probes to the immobilized NAMs;

(d) detecting immobilized NAMs which hybridize weakly to a labeled probe;

(e) determining the sequence of the immobilized molecule of step (d);

(f) comparing the sequence of the immobilized sample to one or more

sequences in a sequence database; and
(g) determining whether the NAM is identical to one or more of the database sequences. An immobilized sequence of step (e) which shows homology with, but is not identical to, sequences in the database, is a nucleic acid sequence related to a known sequence;
(8) removing undesired sequences from a sample of NAMs, comprising:
(a) immobilizing a heterogeneous sample of NAMS on a solid surface in a microarray format;
(b) hybridizing labeled probes to the immobilized NAMs, where the labeled probes include a sequence whose removal is desired from the sequence;
(c) identifying at least one NAM which hybridizes weakly, or does not hybridize, to the labeled probe;
(d) determining the sequence of the NAM of step (d); and
(e) reiterating steps (a)-(d) or (b)-(d), thus eliminating unwanted sequences from the population of NAMs.
(9) identifying changes in copy number of DNA sequences between a first NAM population and a second NAM population, comprising:
(a) immobilizing a sample of heterogeneous NAMS on a solid surface in a microarray format;
(b) hybridizing labeled probes from a first and second population to the immobilized NAMs;
(c) detecting NAMs which show absent, significantly less or significantly greater hybridization to a labeled probe from the first population, relative to labeled probes from the second population; and
(d) determining the sequence of the NAMs identified in (c), thus identifying changes in copy number of DNA sequences between different sources of NAMs.
USE - The processes are useful for identification and elimination of redundancy in NAM populations. They can also be used for removal of contaminating NAMs from cloning libraries, or for isolation and/or enrichment of DNA sequences that are unique to one population. They can also be used for enhancing the rate of discovery of genomic sequences and facilitating isolation of DNA fragments corresponding to a whole genome or subregions of interest.
ADVANTAGE - The processes are highly efficient and high throughputs can be achieved. They typically involve a reiterative subtractive protocol that becomes more biased towards unknown genes with each successive round. The removal of repetitive and previously characterized NAMs from the library allows identification of low abundance mRNA from sources of interest and enhances the rate of novel gene discovery.
Dwg.0/4

TECH UPTX: 20010116
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Process: the sample of NAMs comprises DNA (especially cDNA or genomic DNA) or RNA. The DNA can be a clone from a library. The NAMs in the sample are amplified, especially by polymerase chain reaction (PCR). The label is a fluorescent label, a luminescent label or a radioactive label. The labeled probes are cDNA/mRNA or genomic sequences.

L49 ANSWER 64 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2001-024873 [03] WPIX
DNC C2001-007587
TI Nucleic acid sequencing and quantitation, using the same reagents for both assays, e.g. for detection of viral infection or diagnosis of cervical intraepithelial neoplasia.
DC B04 D16
IN AUGUST, M J; YAGER, T D
PA (VISI-N) VISIBLE GENETICS INC
CYC 22
PI WO 2000068410 A1 20001116 (200103)* EN 35p <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US

AU 2000048365 A 20001121 (200112) <--
ADT WO 2000068410 A1 WO 2000-US12822 20000508; AU 2000048365 A AU 2000-48365 20000508
FDT AU 2000048365 A Based on WO 200068410
PRAI **US 1999-133168P 19990507**
AN 2001-024873 [03] WPIX
AB WO 200068410 A UPAB: 20010116

NOVELTY - Simultaneous sequencing and quantitation of a target nucleic acid (TNA) analyte in a sample, using the same reagents for both assays, is carried out by processing the sample through a plurality of thermocycles to give a mixture of labeled polynucleotide fragments which are used for determining both sequencing information and the amount of TNA present.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) simultaneous sequencing and quantitation of a TNA analyte in a sample, comprising:

(a) processing the sample using a single set of reagents (which includes at least one labeled reagent for labeling the TNA or a product derived from the TNA), through a plurality of thermocycles, to obtain a mixture of labeled polynucleotide fragments derived from the TNA, these fragments are used for determination of both sequence information about the TNA and the amount of TNA present in the sample. Step (a) is carried out within a quantitative regime;

(b) separating the labeled nucleic acid sequencing fragments in the modified sample on the basis of size, and detecting the label associated with the separated polynucleotide fragments;

(c) evaluating the positions of the separated nucleic acid fragments to obtain information about the sequence of the TNA; and

(d) evaluating the intensity of a signal derived from the label associated with one or more of the separated polynucleotide fragments to determine the quantity of the TNA in the sample;

(2) kit for sequence analysis and quantitation of a TNA in a sample, comprising:

(a) at least one primer pair flanking a region of interest within the TNA, at least one member of the primer pair being labeled with a detectable label;

(b) a thermostable template-dependent DNA polymerase;

(c) feedstock solutions and buffers for performing a thermally-cycled primer extension reaction; and

(d) calibration information specific to the reagents within the kit. The calibration information provides information for correlating the amount of the TNA in the sample with the amount of polynucleotide product produced through the use of the kit; and

(3) kit for sequence analysis and quantitation of a TNA in a sample, comprising:

(a) components (a), (b) and (c) as described in (2);

(b) a reference polynucleotide; and

(c) at least one reference primer pair flanking a region of the reference polynucleotide, at least one member of this primer pair being labeled with a second detectable label which is distinguishable from the first detectable label.

USE - The process is useful for simultaneous sequencing and quantitation of nucleic acid analytes in samples (claimed). It can be used for detection and quantitation of nucleic acid analytes associated with, e.g. human immunodeficiency virus (HIV-1), HIV-2 or human papilloma virus. It may be used for diagnosis of disorders such as HIV infection or cervical intraepithelial neoplasia (of which the presence of human papilloma virus is a predictor).

The full-length product is used for determination of the amount of TNA present in the sample, while the terminated sequencing fragments can be used for determination of both sequencing information about the TNA and the amount of TNA in the sample (claimed).

ADVANTAGE - Only one label is needed for both sequencing and

quantitation, although two or more labels may be used if bidirectional sequencing is performed.
Dwg.0/10

TECH UPTX: 20010116
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Process: The process also comprises, prior to step (a), amplifying the TNA in the sample.
The TNA is an RNA, and the process can also comprise reverse transcribing the RNA target to produce a cDNA template prior to step (a). Step (a) is carried out within a quantitative regime, i.e. the process is carried out at lower cycle numbers where a plot of the amount of product as a function of cycle is linear.
An internal polynucleotide standard can be added to the sample in a known amount, and coprocessed in the same reaction vessel to produce a detectable reference product. The intensity of a signal derived from the reference product is then compared to the signal derived from the label associated with the separated fragments, to determine the quantity of the TNA in the sample.
The sample can be processed in two parallel replicate reactions to produce both full-length product and terminated polynucleotide sequencing fragments. The two reactions include a first reaction which is stopped after a first number of thermal cycles, so that the production of the full-length product is within a quantitative regime, and a second reaction which is stopped after a second number of thermal cycles (greater than the first number), so that the production of sequencing fragments is within a quantitative regime.

L49 ANSWER 65 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-674084 [66] WPIX
DNC C2000-204438
TI New oligonucleotides primers, bumpers and detector probes for detecting and identifying Salmonella spp. , and for amplifying target sequences found in Salmonella spp. .
DC B04 D16
IN HELLYER, T J; MCMILLIAN, R A; ROSTKOWSKI, C A; ZAGOURAS, P
PA (BECT) BECTON DICKINSON & CO
CYC 28
PI EP 1045032 A2 20001018 (200066)* EN 21p <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CA 2302872 A1 20001012 (200066) EN <--
US 6165721 A 20001226 (200103) <--
JP 2000342282 A 20001212 (200104) 49p <--
ADT EP 1045032 A2 EP 2000-104804 20000306; CA 2302872 A1 CA 2000-2302872 20000411; US 6165721 A US 1999-289380 19990412; JP 2000342282 A JP 2000-110095 20000412
PRAI **US 1999-289380 19990412**
AN 2000-674084 [66] WPIX
AB EP 1045032 A UPAB: 20001219
NOVELTY - New oligonucleotides comprising an oligonucleotide consisting of the target binding sequences SAL1LA1, SAL1LA2, SAL1LA3, SAL1RA1, SAL1RA2, 2SalAL46 or 2SalR46, and optionally a sequence required for an amplification reaction, bumper primers SAL1LB1, SAL1LB2, SAL1RB1, SAL1RB2, SALIRB2', 2SalBL48 or 2SalBR48, detector probes SAL1EXTA or SAL1EXTB, or a nucleic acid complementary to SAL1EXTA or SAL1EXTB, are new.
DETAILED DESCRIPTION - The oligonucleotides comprise the following sequences:
(1) SAL1LA1 - cgattccgct ccagacttct cggggaaaaa gttaggtcat ttc;
(2) SAL1LA2 - cgattccgct ccagacttct cgggcgaaaa agttaggtca t;
(3) SAL1LA3 - cgattccgct ccagacttct cgggtacgcg aaaaagttag g;
(4) SAL1RA1 - accgcatcga atgcatgtct cggggatatg ttgaatatct aacg;
(5) SAL1RA2 - accgcatcga atgcatgtct cggggaatat ctaacgtttc cac;
(6) 2SalAL46 - cgattccgct ccagacttct cgggacattg caacatgaca t;
(7) 2SalAR46 - accgcatcga atgcatgtct cggggcgcct tattacctg;

(8) SAL1LB1 - gcggaagttt attgct;
(9) SAL1LB2 - cccgtgcgga agtt;
(10) SAL1RB1 - cagttgtatt attttcttc;
(11) SAL1RB2 - ttattttctt cttcgatatg;
(12) SAL1RB2' - attattttct tcttcgata;
(13) 2SalBL48 - ttgatattac agtatatgg;
(14) 2SalBR48 - gacaggatca aaacaag;
(15) SAL1EXTA - accgtgttga aggggg;
(16) SAL1EXTB - aataattccc ccttcaac; and
(17) Salm2ExtB - caaacactaa atcatcca.

INDEPENDENT CLAIMS are also included for the following:

(1) a kit comprising:

(a) one or more primers selected from SAL1LA1, SAL1LA2, SAL1LA3;

(b) one or more primers selected from SAL1RA1, or SAL1RA2;

(c) bumpers SAL1B1 or SAL1LB2, and SAL1RB1, SAL1RB2 or SALRB2'; and

(d) one or more detectors selected from SAL1EXTA, SAL1EXTB, or their complement;

(2) a kit comprising primer 2SalAL46 and 2SalAR46, bumpers 2SalBL48 and 2SalBR48, and a detector Salm2ExtB or its complement;

(3) detecting the presence of Salmonella in a sample by:

(a) treating the sample using a pair of nucleic acid primers in a nucleic acid amplification reaction where the first primer is SAL1LA1, SAL1LA2 or SAL1LA3, and the second primer is SAL1RA1, SAL1RA2 or the first primer is 2SalAL46 and the second primer is 2SalAR46; and

(b) detecting any amplified nucleic acid product, which indicates the presence of Salmonella; and

(4) amplifying a target nucleic acid sequence of Salmonella spp. by:

(a) hybridizing to the nucleic acid a first amplification primer consisting of the target binding sequence SAL1LA1, SAL1LA2 or SAL1LA3, a second amplification primer consisting of the target binding sequence SAL1RA1 or SAL1RA2, and optionally a sequence required for the amplification reaction, or a first amplification primer consisting of the target binding sequence 2SalAL46, a second amplification primer consisting of the target binding sequence 2SalAR46, and optionally a sequence required for the amplification reaction; and

(b) extending the hybridized first and second amplification primers on the target nucleic acid sequence, where the target nucleic acid sequence is amplified.

USE - The oligonucleotide primers are used for amplification of target sequences, specifically those found in Salmonella spp. These oligonucleotides may be used after culture as a means for confirming the identity of the culture organism, in clinical samples from humans or animals or with samples of contaminated food or water for detection and identification of Salmonella spp. nucleic acid using known amplification methods.

ADVANTAGE - These oligonucleotides and assay methods provide a means for rapidly differentiating or discriminating between Salmonella spp. and other microorganisms.

Dwg.0/0

TECH UPTX: 20001219

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Sequence: The sequence required for the amplification reaction is a restriction endonuclease recognition site which is nicked by a restriction endonuclease during Strand Displacement Amplification.

Preferred Method: Detecting the amplified nucleic acid product is conducted by hybridizing the amplified nucleic acid product with a detector, where the detector is SAL1EXTA, SAL1EXTB, Salm2ExtB, or their complement. The amplification reaction or the detection of the amplified product, or both utilizes an electronic microarray. Amplifying a target nucleic acid sequence of Salmonella further comprises detecting the amplified target nucleic acid by hybridization to the detector probe SAL1EXTA or SAL1EXTB tagged with a detectable label.

L49 ANSWER 66 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-657765 [64] WPIX
CR 2002-134193 [05]
DNC C2000-199158
TI Determining the concentration of a target nucleic acid, useful e.g. for detecting genetic mutations, comprises using a fluorescently labeled probe in which emission is reduced by binding to the target nucleic acid.
DC B04 D16
IN FURUSHO, K; KAMAGATA, Y; KANAGAWA, T; KOYAMA, O; KURANE, R; KURATA, S; YAMADA, K; YOKOMAKU, T
PA (AGEN) AGENCY OF IND SCI & TECHNOLOGY; (NIBI-N) JAPAN BIOINDUSTRY ASSOC; (KANK-N) KANKYO ENG CO LTD; (FURU-I) FURUSHO K; (KAMA-I) KAMAGATA Y; (KANA-I) KANAGAWA T; (KOYA-I) KOYAMA O; (KURA-I) KURANE R; (KURA-I) KURATA S; (YAMA-I) YAMADA K; (YOKO-I) YOKOMAKU T
CYC 27
PI EP 1046717 A2 20001025 (200064)* EN 55p <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CA 2304260 A1 20001020 (200066) EN <--
US 2001000148 A1 20010405 (200120) <--
US 2001000175 A1 20010405 (200120)
EP 1046717 A9 20010627 (200137) EN <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT EP 1046717 A2 EP 2000-108643 20000420; CA 2304260 A1 CA 2000-2304260 20000420; US 2001000148 A1 Div ex US 2000-556127 20000420, US 2000-725256 20001129; US 2001000175 A1 Div ex US 2000-556127 20000420, US 2000-725265 20001129; EP 1046717 A9 EP 2000-108643 20000420
PRAI **JP 1999-111601 19990420**
AN 2000-657765 [64] WPIX
CR 2002-134193 [05]
AB EP 1046717 A UPAB: 20020319
NOVELTY - Determination of the concentration of a nucleic acid target (I) uses a fluorescently labeled probe (II) which produces reduced fluorescence emission when hybridized to (I) and comprises measuring the reduction in emission caused by hybridization.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a probe (IIa) labeled with a fluorescent dye at its end and designed so that, when hybridized, at least one G residue is present in (I) at 1 - 3 bases from the end where (I) and (IIa) are hybridized;

(2) a probe (IIb) similar to (IIa) but designed so that when hybridized, bases present in (I) and (IIb) form at least one GC pair at the labeled end;

(3) determining the concentration of (I) by hybridization to (IIa) or (IIb) and measuring reduction in fluorescent emission;

(4) a kit for analyzing or detecting polymorphisms and mutations in (I), using (IIa) or (IIb);

(5) a method for analyzing data from method (3);

(6) a system for performing method (5);

(7) a device for determining the concentration of (I) comprising a solid support having on its surface:

(i) (IIa) or (IIb); or

(ii) some other probe (IIc) that contains two different fluorescent dyes that are quenched in one of the hybridized or non-hybridized conditions but able to emit in the other condition;

(8) determining the concentration of (I) using the device of (7); and

(9) a method for analyzing the melting curve of (I).

USE - The new method is particularly used to quantify (I) by a real-time polymerase chain reaction, e.g. for quantifying microbial cells in co-cultures or symbiotic systems, for detecting gene mutations or polymorphisms, and for analyzing melting curves of (I) to determine a Tm value.

ADVANTAGE - (I) can be quantified quickly, easily and accurately. Particularly there is no need to remove unbound probe; no materials are introduced that inhibit amplification by Taq polymerase (so conventional PCR conditions can be used); the specificity of PCR is kept high (amplification of primer dimers is delayed) and the limit of quantitation is reduced; complex probes are not needed and amplification can be monitored in real time. The working graph for data analysis (automatically generated by a computer) has a higher correlation coefficient than conventional graphs so more accurate quantitation is possible.
Dwg.0/21

TECH UPTX: 20001209
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Probes: (IIa) and (IIb) are labelled at 3' or 5'-ends, and in (IIb) the labeled end base is C or G. When the label is at the 3'-end, a hydroxy group at position 2' or 3' in ribose or 3' in deoxyribose, at the 3'-end of the probe, may be phosphorylated. All probes may be chemically modified, and are particularly ribonucleoside/deoxyribonucleoside chimeras, with the ribonucleosides 2'-O-methylated.
Preferred Materials: (I) is particularly RNA and may be purified from a microorganism or animal, or present in cultured cells or cell homogenates.
Preferred Process: A helper probe may be added before hybridization of (I) and (II) and/or (I) is first heated to degrade higher order structure. Particularly the method is used in a polymerase chain reaction (PCR), specifically quantitative real-time PCR. Processing of the results includes correction of the fluorescence values and equations presented for doing this. Particularly the amplification mixture is heated until complete denaturation is achieved, with measurement of fluorescence at predetermined intervals during heating. The results are plotted as a melting curve and this differentiated to give values for the rate of change of fluorescence with time. The differential values are then displayed and a point of inflection identified.
Preferred Device: The device of (7) has many probes bound in an array, each probe having a temperature sensor and heating element, on opposite surfaces of the solid support, to provide optimal temperature.

TECHNOLOGY FOCUS - COMPUTING AND CONTROL - Preferred System: The system of (7) is a computer-readable memory containing appropriate programs.

L49 ANSWER 67 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-657762 [64] WPIX
DNN N2000-487677 DNC C2000-199155
TI Solid-phase labeling of nucleic acid, useful e.g. in DNA hybridization analysis using microarrays, comprises transamination of cytidine to introduce reactive group, then attaching label.
DC B04 D16 **S03**
IN CRUICKSHANK, K A
PA (VYSI-N) VYSIS INC
CYC 27
PI EP 1046649 A1 20001025 (200064)* EN 14p <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2000300299 A 20001031 (200105) 11p <--
US 6194563 B1 20010227 (200114) <--
ADT EP 1046649 A1 EP 2000-302412 20000324; JP 2000300299 A JP 2000-85490 20000327; US 6194563 B1 US 1999-277087 19990326
PRAI **US 1999-277087 19990326**
AN 2000-657762 [64] WPIX
AB EP 1046649 A UPAB: 20001209
NOVELTY - Method for attaching a label to nucleic acid (I) by binding (I), containing a cytidine (C) base, to a solid support; transaminating C with a reactive group (RG) to form a covalent link between RG and C, and linking the label to RG.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the

following:
(a) a composition comprising (I), linked to a solid support, that includes a label linked to RG that is covalently bonded to C; and
(b) kits comprising solid support, a bisulfite, RG and a label.
USE - The method is used to label (I) for use in DNA analysis (by hybridization), particularly in preparation of microarrays.
ADVANTAGE - The method provides efficient functionalization with RG for subsequent labeling and is quicker (over a few hours) than similar processes carried out in solution, making it suitable for automated/robotic labeling of many (I).
Dwg.0/0

TECH UPTX: 20001209
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Materials: The support is a bead or chromium-plated glass slide. RG is of formula -N(R1)-R-X- or preferably of formula NH2(CH2CH2X')nCH2CH2NH2, or is a peptide with pre-attached fluorophore -N(R1)-R-X-.
R = 2-14C alkylene;
X = NR2 or COO;
R1, R2 = H or lower alkyl;
X' = oxygen, sulfinyl, sulfonyl, silicon or N(lower alkyl); and
n = 1-4.
The label is a fluorophore and (I) has 1-2 kb. (I) is covalently linked to the support, especially by reacting a terminal phosphate with an amino-functionalized support in presence of 1-ethyl-3-(dimethylaminopropyl) carbodiimide. This bond is stable to labeling conditions but can be broken at high pH (for recovering DNA) or by heat-treatment with formamide (for recovering RNA).
Preferred process: Transamination is catalyzed by bisulfite. RG is dissolved in a solution containing a trihaloacetate (specifically trifluoroacetate) chaotropic anion, and after reaction the modified (I) is released from its support.

L49 ANSWER 68 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-656331 [63] WPIX
DNN N2000-486529 DNC C2000-198677
TI Amplifying specific target nucleic acids in mixed sample, used in rapid analysis methods, comprises introducing nucleic acids onto bioelectronic microchip.
DC B04 D16 **J04** S05 U12 U13 U14
IN EDMAN, C F; NERENBERG, M I; NERENBURG, M I
PA (NANO-N) NANOGEN INC; (BECT) NANOGEN/BECTON DICKINSON PARTNERSHIP; (EDMA-I) EDMAN C F; (NERE-I) NERENBURG M I
CYC 22
PI WO 2000061816 A1 20001019 (200063)* EN 134p <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
US 6326173 B1 20011204 (200203)
EP 1171635 A1 20020116 (200207) EN <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 2000061816 A1 WO 2000-US9700 20000411; US 6326173 B1 US 1999-290338 19990412; EP 1171635 A1 EP 2000-922077 20000411, WO 2000-US9700 20000411
FDT EP 1171635 A1 Based on WO 200061816
PRAI **US 1999-290338 19990412**
AN 2000-656331 [63] WPIX
AB WO 200061816 A UPAB: 20001205
NOVELTY - Amplifying specific target nucleic acids in a mixed sample, comprising introducing nucleic acids onto a bioelectronic microchip having electronically addressable capture sites, electronically addressing the nucleic acids to sites which are connected to specific capture probes, hybridizing the nucleic acids and amplicons to the probes, and performing sequence based amplification, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) amplifying specific target nucleic acids in a mixed sample, comprising:
(a) introducing the nucleic acids onto a bioelectronic microchip having electronically addressable capture sites;
(b) electronically addressing the nucleic acids to specific capture sites which are connected to specific capture probes;
(c) performing sequence-based amplification in a solution above the capture sites, to form amplicons of the target; and
(d) electronically hybridizing the target nucleic acids and amplicons to the probes;
(2) amplification, multiplex assaying, and detection of target nucleic acids in mixed sample using a bioelectronic microchip, comprising:
(a) introducing at least one of the nucleic acids onto a bioelectronic microchip having electronically addressable capture sites;
(b) electronically addressing the nucleic acids to the capture sites;
(c) amplifying the nucleic acids to form amplicons of the target nucleic acids;
(d) electronically addressing the amplicons to the capture sites;
(e) capturing the amplicons and target nucleic acids onto the capture sites to which they are addressed by capture probes; and
(f) detecting the presence of the captures amplicons and the targets; and
(3) a kit for carrying out nucleic acid sequence based amplification (NASBA)-based strand displacement amplification (SDA) reactions for use on a bioelectronic microchip, comprising one or more oligonucleotides specific for Factor V, Hemochromotosis, or a bacterium, the oligonucleotides comprise amplification primers, bumper primers, capture probes, and/or signal probes selected from one of 62 sequences, all fully defined in the specification.
USE - For use in unified amplification-hybridization-detection methods used in rapid analysis of mixed nucleic acid samples (claimed).
ADVANTAGE - The novel method uses strand displacement amplification which is an isothermal technique that requires simpler thermal control than polymerase chain reaction, making it more suitable for use in microarrays using microchips. The system can be used in unified amplification-hybridization-detection systems for more rapid analysis. Multiple, different nucleic acid samples can be simultaneously amplified on one array.
Dwg.0/24

TECH UPTX: 20001205
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The electronic addressing includes the passing of a negative charge through an electrode associated with the capture sites to create electronically induced stringency to remove mis-matched hybridization between the capture probes and non-target nucleic acids in the sample. The addressing is used to enhance nucleic amplification for forming amplicons in amplification reactions selected from polymerase chain reaction, SDA, allele-specific SDA, anchored SDA, amplification, ligation-based SDA and NASBA. The novel method further comprises thermally, or electronically, denaturing the nucleic acids and amplificons on the capture sites after amplification. The capture probes serve as primers for the amplification, and are preferably biotinylated. The method further comprises introducing a target specific reporter oligonucleotide during, or after amplification of the target nucleic acid. In the method of (2), the amplification is NASBA, and is carried out using anchored or non-anchored primers. The amplification, multiplex assaying and detecting are carried out consecutively, or simultaneously. The detection of amplicons is by fluorescence, chemiluminescence and/or electrochemiluminescence. Non-cleavable primers are used for the amplification.
Preferred Kit: The signal probes are detectably labeled.

L49 ANSWER 69 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-648880 [63] WPIX

DNC C2000-196320
TI Nucleic acid analysis method comprises using a control module to determine the need for a second hybridization reaction based on results from a first hybridization reaction.
DC B04 D16
IN ROGERS, C; ROGERS, C H
PA (INMR) BIOMERIEUX INC
CYC 32
PI EP 1045036 A2 20001018 (200063)* EN 20p <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2000316560 A 20001121 (200064) 20p <--
AU 2000026408 A 20001116 (200065) <--
CA 2302067 A1 20001013 (200065) EN <--
US 6225067 B1 20010501 (200126) <--
US 6235479 B1 20010522 (200130) <--
BR 2000001587 A 20010814 (200154) <--
KR 2001020731 A 20010315 (200159) <--
MX 2000003199 A1 20010101 (200166)
AU 741530 B 20011206 (200206) <--
ADT EP 1045036 A2 EP 2000-302976 20000407; JP 2000316560 A JP 2000-112632 20000413; AU 2000026408 A AU 2000-26408 20000405; CA 2302067 A1 CA 2000-2302067 20000323; US 6225067 B1 Div ex US 1999-291566 19990413, US 1999-443027 19991118; US 6235479 B1 US 1999-291566 19990413; BR 2000001587 A BR 2000-1587 20000412; KR 2001020731 A KR 2000-19218 20000412; MX 2000003199 A1 MX 2000-3199 20000331; AU 741530 B AU 2000-26408 20000405
FDT AU 741530 B Previous Publ. AU 200026408
PRAI **US 1999-291566 19990413; US 1999-443027 19991118**
AN 2000-648880 [63] WPIX
AB EP 1045036 A UPAB: 20001205
NOVELTY - A novel method for performing nucleic acid analysis.
DETAILED DESCRIPTION - A novel method for performing nucleic acid analysis comprises:
(a) conducting a first hybridization reaction with a target nucleic acid or its complementary sequence from a test sample;
(b) generating a signal from the first hybridization reaction;
(c) supplying the signal to a control module;
(d) processing the signal in the control module to determine whether the signal is greater than a threshold level;
(e) if the signal is greater than the threshold level, transferring the target nucleic acid or its complementary sequence to a device for (f) conducting a second hybridization reaction;
(f) generating a signal from the second reaction; and
(g) processing the signal in the control module to analyze the target nucleic acid.
INDEPENDENT CLAIMS are also included for the following:
(1) an integrated instrument system for automated nucleic acid analysis, comprising:
(a) a sample processing station for providing one or more target nucleic acid sequences from a test sample;
(b) a first test reaction station for performing a first hybridization reaction on one or more of the target nucleic acid sequences or their complementary sequences, the first reaction comprising a low detection format device having 1-10 discrete nucleic acid sequences;
(c) a second reaction station for performing a second hybridization reaction on one or more of the target nucleic acid sequences or their complementary sequences, the second reaction comprising a high detection format device having more than 100 discrete nucleic acid sequences;
(d) at least one detector for determining positive hybridization detection signals for the target nucleic acid sequences or their complementary sequence in the first or second hybridization reactions; and
(e) a control module for integrated operation of the instrument, where the module determines the need for performance of the second

hybridization reaction based on the results from the detector and for analysis of detection signals from the first and second hybridization reactions;

(2) a method for conducting a nucleic acid analysis, comprising:

(a) amplifying all target nucleic acid sequences in a test sample and internal control sequences which are needed for limited and multi-detection analysis;

(b) performing a limited detection analysis of one or more amplified nucleic acid sequences;

(c) measuring internal control signals and target signals from the limited detection analysis;

(d) supplying the internal control signals and the target signals to a control module;

(e) implementing a control algorithm in the control module, the algorithm:

(i) comparing the internal control signals with a first threshold value, the comparison determining whether to reject the test and if the comparison indicates that the test is not rejected; and

(ii) comparing the target signals with a second threshold; and

(f) transferring the previously amplified nucleic acid sequence(s) to a multi-detection device and conducting the multi-detection assay in the device;

(3) a diagnostic method for data collection from a test sample containing one or more nucleic acid sequences on an automated instrument, comprising:

(a) releasing nucleic acid sequences from a test sample;

(b) amplifying the nucleic acid sequences to produce amplicons;

(c) providing the amplicons to a low detection format comprising complementary nucleic acid sequences to one or more of the amplicons for a hybridization reaction;

(d) detecting the presence of the amplicons hybridized by the low detection format; and

(e) determining by control algorithm a positive or negative result in step (c), where the amplicons from step (b) are further analyzed in a high detection format for data collection if a positive result has been obtained.

USE - The method is useful for testing analytical or biological samples, e.g. for identifying microorganisms or viruses and/or determining their sensitivity or resistance to drugs.

ADVANTAGE - On the basis of the results from a first hybridization reaction using few probes (low detection format), the control module determines if there is a need for a second hybridization reaction using many probes (high detection format).

Dwg.0/7

TECH UPTX: 20001205

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The second reaction comprises a high detection format comprising more than 100 (especially more than 1000) nucleic acid sequences, preferably having a spatial density greater than 400 nucleotides/cm2. The method further comprises simultaneously amplifying selected target nucleic acid sequences and internal control nucleic acid sequence, measuring a signal from the internal control, comparing the internal control signal with a threshold value for the internal control, and rejecting the test if the internal control signal is less than the internal control threshold value.

Preferred Instrument: The instrument further comprises a second detector for detecting positive hybridization reaction signals of the target nucleic acid sequences or their complementary sequences on the high detection format and the high detection format provides further data for the target nucleic acid sequences. The sample processing station further comprises means for preparing selected target nucleic acid sequences and/or means for performing a nucleic acid amplification process on the target nucleic acid sequences provided from step (a) and/or means for providing of internal control nucleic acid sequences. The instrument

further comprises a fluidic transfer means from the sample processing station to the first test reaction station and/or from the first test reaction station to the second reaction station as determined by the control module, preferably automatically and without human intervention and without allowing contact between fluids being transferred and the external environment. The low detection format device provides means for performing a homogenous solution hybridization reaction and the high detection format device provides means for performing a matrix hybridization reaction. The control module selects the use of one or more high detection formats based on the results of the detection signal(s) data from the first hybridization reaction. The amplification process is TMA, PCR, NASBA, SDA or LCR. The low and high detection formats are disposable devices.

L49 ANSWER 70 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-620335 [60] WPIX
DNC C2000-185967
TI New oligonucleotide primers, useful for detection of Yersinia enterocolitica by amplification, provide rapid, selective and sensitive diagnosis.
DC B04 D16
IN FORT, T L; YOU, Q
PA (BECT) BECTON DICKINSON & CO
CYC 28
PI EP 1045031 A2 20001018 (200060)* EN 16p <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CA 2303303 A1 20001012 (200060) EN <--
JP 2000342283 A 20001212 (200104) 17p <--
US 6197514 B1 20010306 (200115) <--
ADT EP 1045031 A2 EP 2000-104320 20000302; CA 2303303 A1 CA 2000-2303303 20000411; JP 2000342283 A JP 2000-110096 20000412; US 6197514 B1 US 1999-289752 19990412
PRAI **US 1999-289752 19990412**
AN 2000-620335 [60] WPIX
AB EP 1045031 A UPAB: 20001123
NOVELTY - Oligonucleotides (ON1) comprising a target-binding sequence (TBS) that is any of 6 specified sequences and optionally a sequence (S) required for an amplification reaction, are new.

DETAILED DESCRIPTION - Novel oligonucleotides (ON1) comprise a target-binding sequence (TBS) that is any of 6 specified sequences and optionally a sequence (S) required for an amplification reaction.

The TBS sequences are: 5'-CGATTCCGCTCCAGACTTCTCGGGQ1 or 5'-ACCGCATCGAATGCATGTCTCGGGQ2

Q1 = AGGTATACAAGCAAGCT (1); AGGTATACAAGCAAGC (2) or AGGTATACAAGCAAG (3) and

Q2 = CAATCCCAATCACTACT (4), CAATCCCAATCACTAC (5) or CAATCCCAATCACTA (6).

INDEPENDENT CLAIMS are also included for the following:

(a) the bumper oligonucleotides (ON2) (7) and (8);

(b) the detector probes (ON3) (9) and (10), or their complements;

(c) kits containing one or more each of (1)-(3) and (4)-(6), plus (7), (8) and one or more ON3;

(d) method for detecting Yersinia enterocolitica by amplification with a pair of ON1 and detection of the amplicon; and

(e) method for amplifying target nucleic acid in Y. enterocolitica using ON1.

5'-ACACCAATAACCGCT (7)
5'-GATTGCAACATACATC (8);
5'-CCACCACCCGAAGTC (9)
5'-GACTTCGGGTGGTGG (10);

USE - ON1 are primers for specific amplification of Yersinia enterocolitica, with subsequent detection of the amplicon for detecting

the bacterium (which causes hemorrhagic enterocolitis, terminal ileitis, mesenteric lymphadenitis and septicemia) in patient samples, food and water, also for confirming identity of cultured cells.

ADVANTAGE - ON1 provide rapid, efficient and specific amplification and detection.

Dwg.0/0

TECH UPTX: 20001123

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Oligonucleotides: In ON1, sequence (S) is a restriction endonuclease (RE) recognition site that is nicked by RE during strand displacement amplification (SDA). ON1 are derived from sequences in the yst gene and can be used for high temperature (thermophilic SDA or polymerase chain reaction) or low temperature (SDA, self-sustained sequence replication, nucleic acid sequence-based amplification or transcription-based amplification system) amplification methods. In (1)-(6), the central CTCGGG motif is a BsoBI recognition site and Q1/Q2 is the TBS.

Preferred Process: In method (d), the amplicon is detected by hybridization with ON3, particularly labeled. Especially amplification and/or detection is (are) performed on an electronic microarray.

L49 ANSWER 71 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-611523 [58] WPIX
CR 1997-100216 [09]; 2000-021736 [02]; 2000-655615 [63]; 2002-254270 [30]; 2002-453565 [48]
DNC C2000-182987
TI New electrodes comprising metal complexes capable of acting as electropolymerization initiators and a mediators for base oxidation, for the electrochemical detection of hybridized nucleic acid containing guanine moieties.
DC A96 B04 D16
IN ONTKO, A C; THORP, H H
PA (UYNC-N) UNIV NORTH CAROLINA
CYC 87
PI WO 2000055366 A1 20000921 (200058)* EN 38p <--
    RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
        OA PT SD SE SL SZ TZ UG ZW
    W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
        GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
        MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
        UA UG US UZ VN YU ZA ZW
   AU 2000029835 A 20001004 (200101) <--
   US 6180346 B1 20010130 (200108) <--
   NO 2001004429 A 20011109 (200203) <--
   EP 1161560 A1 20011212 (200204) EN <--
    R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
        RO SE SI
   KR 2001104724 A 20011126 (200231) <--
   CN 1343260 A 20020403 (200247) <--
ADT WO 2000055366 A1 WO 2000-US3110 20000204; AU 2000029835 A AU 2000-29835 20000204; US 6180346 B1 CIP of US 1995-495817 19950627, CIP of US 1996-667337 19960620, CIP of US 1996-667338 19960620, CIP of US 1997-950503 19971014, US 1999-267552 19990312; NO 2001004429 A WO 2000-US3110 20000204, NO 2001-4429 20010912; EP 1161560 A1 EP 2000-908508 20000204, WO 2000-US3110 20000204; KR 2001104724 A KR 2001-711551 20010911; CN 1343260 A CN 2000-804705 20000204
FDT AU 2000029835 A Based on WO 200055366; US 6180346 B1 CIP of US 5871918; EP 1161560 A1 Based on WO 200055366
PRAI **US 1999-267552 19990312; US 1995-495817 19950627 ; US 1996-667337 19960620; US 1996-667338 19960620; US 1997-950503 19971014**
AN 2000-611523 [58] WPIX
CR 1997-100216 [09]; 2000-021736 [02]; 2000-655615 [63]; 2002-254270 [30]; 2002-453565 [48]

AB WO 200055366 A UPAB: 20020730
NOVELTY - An electrode useful for the electrochemical detection of a nucleic acid, comprising a thin film containing a metal complex capable of acting both as an electropolymerization initiator and a mediator for the oxidation of a preselected base in the nucleic acid and a functionalized moiety to which the nucleic acid can be attached, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparing an electrode useful for the electrochemical detection of nucleic acids (M1), comprising:

(a) electropolymerizing a film on an electrode where the film comprising a copolymer of a mediator and a functionalized moiety having a carboxylate group; and

(b) attaching an oligonucleotide probe covalently to the film;

(2) an electrode (E2) useful for the electrochemical detection of a preselected base in a nucleic acid, comprising:

(a) a substrate having a conductive working surface; and

(b) an electropolymerized film on the conductive working surface where the electropolymerized film comprises a co-polymer of a mediator and a functionalized moiety having a carboxylate group; and

(3) determining the presence of a target nucleic acid in a sample (M2), comprising:

(a) contacting an electropolymerized film comprising a co-polymer of a mediator and a functionalized moiety having a carboxylate group with a sample suspected fo containing a target nucleic acid, with an oligonucleotide probe, where the target and probe form a hybridized nucleic acid on the film;

(b) detecting the oxidation-reduction reaction; and

(c) determining the presence or absence of the nucleic acid from the detected oxidation-reduction reaction.

MECHANISM OF ACTION - In the presence of guanine containing moieties a dramatic enhancement in the oxidative current for the Ru couple (present in the polymeric thin film) due to the catalytic oxidation of guanine is observed.

USE - The electrodes and methods allow the detection of electronic signals associated with nucleic acid hybridization by the detection of aqueous GMP, poly(G) and the surface immobilized single-stranded DNA probes. Any test sample may be used including biopsy samples and biological fluids such as blood, sputum, urine and semen samples, bacterial cultures, soil samples and food samples.

ADVANTAGE - The electrochemical detection of nucleic acids provides an alternative to fluorescent bioassay techniques which eliminates the need for labeling. Guanine nucleobases of polymeric DNA produce an array of redox-active labels suitable for ultrasensitive detection which in conjunction with ultramicroelectrode methods provide a method for detecting many physiologically relevant nucleic acids prior to polymerase chain reaction (PCR) amplification.

DESCRIPTION OF DRAWING(S) - Figures A and B show cyclic voltammograms showing the electropolymerization of (A) poly(Ru(vbpy)32+) and (B) 5:1 poly(Ru(vbpy)32+/vba) from an acetonitrile solution containing 0.1M tetrabutylammonium hexafluorophosphate (TBAH) onto a glassy carbon electrode (100 mV/s scan rate, Ag/AgNO-3 reference). The concentration of Ru(vbpy)32+ in solution was 0.2 mM.

Dwg.1A,1B/8

TECH UPTX: 20001114
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Electrode: The metal complex is poly(Ru(vbpy)3 charge 2+) or poly(Ru(vbpy)3 charge 2+/vba) (where vbpy is 4-vinyl-4'methyl-2,2'-bipyridine and vba is p-vinylbenzoic acid). For the electrode (E2) the mediator is Ru(vbpy)3 charge 2+ and the functionalized moiety is p-vinylbenzoic acid.

Preferred Method: The oligonucleotide probe is attached via a carbodiimide reaction followed by amidation of an amino-linked single-stranded DNA. The mediator is Ru(vbpy)3 charge 2+ and the functionalized moiety is

p-vinylbenzoic acid.

L49 ANSWER 72 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN **2000-516094** [47] WPIX
DNC **C2000-154055**
TI DNA chip comprises solid carrier and oligonucleotide or polynucleotide, which is fixed to carrier in presence of hydrophilic polymer.
DC A96 B04 D16
IN HAKAMATA, M; KUHARA, S; MUTA, S; TASHIRO, K; TSUCHIYA, T
PA (FUJF) FUJI PHOTO FILM CO LTD; (HAKA-I) HAKAMATA M; (KUHA-I) KUHARA S; (MUTA-I) MUTA S; (TASH-I) TASHIRO K; (TSUC-I) TSUCHIYA T
CYC 27
PI EP 1026259 A1 20000809 (200047)* EN 14p <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2000295990 A 20001024 (200059) 9p <--
US 2002090640 A1 20020711 (200248) <--
ADT EP 1026259 A1 EP 2000-102619 20000208; JP 2000295990 A JP 2000-22180 20000131; US 2002090640 A1 Div ex US 2000-499717 20000208, US 2002-53326 20020117
PRAI **JP 1999-30429 19990208**
AN **2000-516094** [47] WPIX
AB EP 1026259 A UPAB: 20000925
NOVELTY - A DNA chip comprises a solid carrier and oligonucleotide or polynucleotide, which is fixed to the carrier in the presence of a hydrophilic polymer.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method of fixing an oligonucleotide or polynucleotide to a solid carrier which comprises spotting an aqueous solution containing the oligonucleotide or polynucleotide and a hydrophilic polymer onto the carrier; and

(2) a process for detecting a DNA fragment complementary to oligonucleotide or polynucleotide fixed to a DNA chip comprising:

(a) spotting an aqueous solution containing the DNA fragment labelled with a fluorescent moiety on the DNA chip, which comprises a solid carrier and oligonucleotide or polynucleotide which is fixed to the carrier in the presence of a hydrophilic polymer;

(b) incubating the spotted chip for performing hybridization between the oligonucleotide or polynucleotide and the complementary DNA fragment in the aqueous solution; and

(c) detecting the hybridized complementary fragment by fluorometry.

USE - The DNA chip is useful in gene analysis.

Dwg.0/2

TECH UPTX: 20000925
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Materials: The oligonucleotide or polynucleotide is fixed to the carrier at one end portion. The solid carrier is coated with poly-L-lysine. The oligonucleotide or polynucleotide has a NH2 terminal and is fixed to the carrier at its NH2 terminal. The hydrophilic polymer is selected from poly(1,4-diazoniabicyclo(2.2.2)octane-1,4-diylmethylene-1,4-phenylenemethylene chloride), polyacrylamide, polyethylene glycol, poly(sodium acrylate), carboxymethylcellulose and albumin. The oligonucleotide or polynucleotide is known in its base sequence. The oligonucleotide or polynucleotide is a synthetically prepared product or a cleaved DNA fragment.
Preferred Methods: The method of (1) further comprises the steps of washing the spotted carrier and drying the washed carrier.

L49 ANSWER 73 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-499119 [44] WPIX
DNN N2000-369965 DNC C2000-149775
TI Detecting nucleic acid in test sample, e.g. for plasmon surface detection; involves incubating solid phase attached to one end of oligonucleotide,

with hairpin structure and fluorophore at free end, with sample for complementary binding.

DC B04 D16 **J04** L03 **S03**

IN CASS, A; STEEL, A; VALAT, C

PA (GENE-N) GENE LOGIC INC; (IMCO-N) IMPERIAL COLLEGE INNOVATIONS LTD

CYC 87

PI WO 2000042222 A2 20000720 (200044)* EN 40p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 2000029655 A 20000801 (200054) <--
US 6312906 B1 20011106 (200170) <--

ADT WO 2000042222 A2 WO 2000-US806 20000114; AU 2000029655 A AU 2000-29655 20000114; US 6312906 B1 Provisional US 1999-116063P 19990115, US 2000-482607 20000114

FDT AU 2000029655 A Based on WO 200042222

PRAI **US 1999-116063P 19990115; US 2000-482607 20000114**

AN 2000-499119 [44] WPIX

AB WO 200042222 A UPAB: 20000913

NOVELTY - A method (I) for detecting the presence of a nucleic acid (II) in a test sample (TS) involves providing a solid phase (S) bound to one end of a oligonucleotide (O) covalently attached to a fluorophore (F) at its other end and comprising at least one hairpin structure between its two ends, incubating TS with (S) for complementary binding of (O) with (II) from TS and detecting the fluorescence from (F).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method (III) for detecting the presence of two or more nucleic acids in TS by providing (S) having two or more (O) using (I) and detecting fluorescence from each of the separate regions of (S);

(2) an analytical test device (IV) for detecting the presence of (II) or two or more nucleic acids in TS comprising (S) with a material that quenches fluorescence and a self-complementary single-stranded oligonucleotide probe linked to the surface of (S) at one of its ends and to (F) at its other end and a hairpin structure between its ends or two or more oligonucleotides bound at separate regions;

(3) a kit (V) for detecting (II) in TS comprising (S) having (O) packaged in a container and instructions for use; and

(4) a fluorescence quenching surface (VI) having at least one type of (O).

USE - The method and oligonucleotide probes are useful for plasmon surface detection and electron transfer detection of one or more nucleic acids.

ADVANTAGE - The probes can be washed and recovered, and are therefore suitable for reuse. Fluorescence for detection is generated upon denaturation of one or more probe hairpin structures and is controlled by distance from a large two dimensional quencher whereas it was necessary to internally label long oligonucleotides probes for the conventional method. The distances can be much larger than those associated with soluble double dye labeled probes.

Dwg.0/4

TECH UPTX: 20000913

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Material: (S) comprises a material which is an electrically or non-electrically conductive polymer, fluorophore labeled protein, metal, metal sheet, metal particle, gold sol, selenium sol, gold plate, platinum plate, doped semiconducting silicon, germanium or selenium, aluminum, silver, platinum, carbon glass, glass or quartz doped with metal ion, glass or quartz doped with a transitional metal ion, iron oxide, chromium oxide, or glass or quartz doped with a lanthanide. (S) further comprises a surface coating of

polymer with covalently attached quenching groups.
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Fluorescence from (F) is detected by exciting (F) with excitation light in an apparatus which provides either total internal reflection of the excitation light or direct excitation. Detected fluorescence is calibrated at a defined temperature before incubation. A signal selection step of applying an electric charge to a part of the solid phase prior to detection is carried out. Preferred Device: (IV) comprises (S) in a flow-through porous form and comprises a micro electronic component at each of the separate regions to permit addressable detection of hybridization. The micro electronic component comprises a separate region of (S) that is bound to (O). (S) is a discontinuous multi-dot metal film in contact with electrophoresis gel surface. (VI) comprises a flat surface upon which multiple oligonucleotides are bound at discrete positions. The oligonucleotide probe is either directly attached to the solid phase through covalent bond or attached indirectly by hybridization with nucleic acid comprising a quenching moiety in the solid phase. The solid phase comprises an array of discrete regions with each region containing a nucleic acid with a quenching moiety.

L49 ANSWER 74 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-375672 [32] WPIX
DNC C2000-113462
TI Nucleic acid arrays for differential gene expression analysis comprise oligonucleotide spots, each corresponding to a target nucleic acid and a oligonucleotide probe composition of several unique oligonucleotides.
DC A96 B04 D16 **J04**
IN CHENCHIK, A
PA (CLON-N) CLONTECH LAB INC; (CHEN-I) CHENCHIK A
CYC 24
PI WO 2000022172 A1 20000420 (200032)* EN 33p <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA IL JP
AU 2000011152 A 20000501 (200036) <--
EP 1121471 A1 20010808 (200146) EN <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 2001055760 A1 20011227 (200206) <--
ADT WO 2000022172 A1 WO 1999-US24070 19991013; AU 2000011152 A AU 2000-11152 19991013; EP 1121471 A1 EP 1999-954927 19991013, WO 1999-US24070 19991013; US 2001055760 A1 Provisional US 1998-104179P 19981013, US 1999-417268 19991013
FDT AU 2000011152 A Based on WO 200022172; EP 1121471 A1 Based on WO 200022172
PRAI **US 1998-104179P 19981013; US 1999-417268 19991013**
AN 2000-375672 [32] WPIX
AB WO 200022172 A UPAB: 20000706
NOVELTY - An array (I) comprising a pattern of oligonucleotide probe spots, each corresponding to a target nucleic acid and comprising an oligonucleotide composition of several unique oligonucleotides, stably associated with the surface of a solid support, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) preparation of (I);
(2) a kit for use in a hybridization assay comprising (I); and
(3) a hybridization assay comprising the steps of:
(a) contacting at least one labeled target nucleic acid sample with a (I) under conditions sufficient to produce a hybridization pattern; and
(b) detecting the hybridization pattern.
USE - (I) is used in an hybridization assay for differential gene expression analysis which involves contacting a labeled target nucleic acid sample with (I) under conditions sufficient to produce a hybridization pattern which is then detected (claimed). (I) is used in the differential gene expression analysis of species specific genes, function specific genes, genes specific for or involved in a particular biological

process, disease associated genes, location specific genes and genes specific genes that change expression level over time. It is also used in drug screening, nucleic acid sequencing, mutation analysis etc.
ADVANTAGE - None given.
Dwg.0/0

TECH UPTX: 20000706
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) is prepared by generating the unique nucleotides followed by stably associating the unique oligonucleotides on the surface of a solid support in a manner sufficient to produce the array (claimed). The method further involves selecting the unique oligonucleotides which are not homologous to any other unique oligonucleotide of any other oligonucleotide probe composition corresponding to a different target nucleic acid.
Preferred Array: (I) comprises a pattern of oligonucleotides spots of a density that does not exceed 400 spots/cm2, each corresponding to a target nucleic acid and comprises an oligonucleotide probe composition made up of 3 - 50 (preferably 3-20) unique oligonucleotides of 15 - 150 (preferably 25-100) nucleotides in length, which are capable of hybridizing to a different region of the corresponding target nucleic acid of the probe oligonucleotides spot in which it is positioned, stably associated with the surface of a solid support. The several unique oligonucleotide hybridize to overlapping or non overlapping regions of a target nucleic acid. The unique nucleotides of each spot co-operatively hybridize to 2-10 or more target nucleic acids represented in the pattern. The array comprises several patterns separated from each other by walls and each probe oligonucleotides spot in the pattern corresponds to a different target nucleic acid. Alternately two or more oligonucleotides spots corresponds to a same target nucleic acid and preferably all the oligonucleotide spots corresponds to the same type of target nucleic acid. The array also comprises the mismatch probe. The density of the spots on the array does not exceed 1000/cm2 and the number of spots range from about 50-10000 (preferably 1000).
Preferred Kit: The kit further comprises reagents for generating a label target nucleic acid sample, a hybridization buffer and a wash medium.
Preferred Assay Method: The hybridization assay method further involves washing the array prior to the detecting step and comprises preparation of a labeled target nucleic acid sample by conjugating a detectable label to a functionalized target nucleic acid sample. The method also involves generating a second hybridization pattern on a same or different array, which are then compared.

TECHNOLOGY FOCUS - POLYMERS - Preferred Solid Support: The solid support may be flexible such as nylon.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Solid Support: The solid support may be rigid such as glass.

L49 ANSWER 75 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-349672 [30] WPIX
CR 2001-289589 [25]
DNC C2000-106339
TI Oligonucleotide primers useful for amplification and detection of nucleic acids of Shigella and Escherichia coli in food, water and clinical samples from human or animals.
DC B04 D16
IN HELLYER, T J; MCMILLIAN, R A
PA (BECT) BECTON DICKINSON & CO
CYC 28
PI US 6060252 A 20000509 (200030)* 14p <--
EP 1044986 A2 20001018 (200053) EN <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CA 2302862 A1 20001012 (200060) EN <--

JP 2000342284 A 20001212 (200104) 17p <--
ADT US 6060252 A US 1999-289750 19990412; EP 1044986 A2 EP 2000-104364 20000302; CA 2302862 A1 CA 2000-2302862 20000411; JP 2000342284 A JP 2000-110097 20000412
PRAI **US 1999-289750 19990412**
AN 2000-349672 [30] WPIX
CR 2001-289589 [25]
AB US 6060252 A UPAB: 20010603
NOVELTY - A kit comprising one or more primers (A) selected from ShH1AL48, ShH1AL46 and ShH1AL44 or ShH1AR50, ShH1AR46 and ShH1AR42, bumpers (B) ShH1BL44 or ShH1BBR44 and one or more detectors (C) selected from ShH1DL44, ShH1DR46 or their complementary sequence, is new.

DETAILED DESCRIPTION - A kit comprising one or more primers (A) selected from ShH1AL48, ShH1AL46 and ShH1AL44 or ShH1AR50, ShH1AR46 and ShH1AR42, bumpers (B) ShH1BL44 or ShH1BBR44 and one or more detectors (C) selected from ShH1DL44, ShH1DR46 or their complementary sequence. ShH1AL48, ShH1AL46, ShH1AL44, ShH1AR50, ShH1AR46, ShH1AR42, ShH1BL44, ShH1BBR44, ShH1DL44 and ShH1DR46 have the following sequence (I)-(X), respectively:

CGATTCCGCTCCAGACTTCTCGGGTCAGAAGCCGTGAAGA (I);
CGATTCCGCTCCAGACTTCTCGGGTCAGAAGCCGTGAAG (II);
CGATTCCGCTCCAGACTTCTCGGGCAGAAGCCGTGAAG (III);
ACCGCATCGAAGTCATGTCTCGGGGCCATGGTCCCCAGA (IV);
ACCGCATCGAAGTCATGTCTCGGGCATGGTCCCCAGAG (V);
ACCGCATCGAAGTCATGTCTCGGGCATGGTCCCCAGA (VI);
GCACTGCCGAAGC (VII);
GCTTCAGTACAGCAT (VIII);
GAATTTACGGACTGG (IX); and
GAACCAGTCCGTAAAT (X).

USE - (A) is useful for detecting and amplifying a target nucleic acid sequence (tNA) of Shigella spp. and enteroinvasive Escherichia coli in a sample. The amplification method comprises hybridizing tNA with (A) and optionally a sequence required for amplification and extending the hybridized primers on the nucleic acid sequence. The optional sequence required for amplification is a recognition site for a restriction endonuclease nicked by the restriction endonuclease during strand displacement amplification (SDA) and the tNA is amplified by polymerase chain reaction (PCR). The detection method comprises treating the sample with (A) in a SDA reaction and detecting any amplified nucleic acid product. The primer pair in both amplification and detection method is preferably ShH1AL48 and ShH1AR46. The SDA reaction is preferably a thermophilic SDA (tSDA) reaction and utilizes (B). The amplified nucleic acid product is detected by contacting with (C) and the amplification, detection or both utilizes an electronic microarray. The tSDA reaction is a homogeneous fluorescent real time reaction (all claimed).

ADVANTAGE - The primers provides methods for rapid discrimination between Shigella spp. and Escherichia coli within a short period of time.
Dwg.0/0
TECH UPTX: 20000624
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Kit: (C) comprises a radioactive or fluorescent marker.

L49 ANSWER 76 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-271085 [23] WPIX
DNN N2000-203058 DNC C2000-082666
TI Rapid screening of large numbers of analytes, e.g. liquid chemical compounds for use as potential drugs, applied to solid support where contacted with targets.
DC A96 B04 D16 **S03**
IN PAUWELS, R W J; ROELANT, C H S; VAN ACKER, K L A
PA (TIBO-N) TIBOTEC NV
CYC 35
PI WO 2000014540 A1 20000316 (200023)* EN 63p <--

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BR CA CN IL JP KR MX NZ PL RU SG TR US
AU 2000022512 A 20000327 (200032) <--
ZA 2000000891 A 20001129 (200106)# 64p <--
BR 9816009 A 20010605 (200138) <--
EP 1112494 A1 20010704 (200138) EN <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU NL PT SE
TW 429312 A 20010411 (200157) <--
CN 1315001 A 20010926 (200206) <--
KR 2001106467 A 20011129 (200234) <--
US 2002081629 A1 20020627 (200245) <--

ADT WO 2000014540 A1 WO 1998-IB1399 19980908; AU 2000022512 A WO 1998-IB1399 19980908, AU 2000-22512 19980908; ZA 2000000891 A ZA 2000-891 20000223; BR 9816009 A BR 1998-16009 19980908, WO 1998-IB1399 19980908; EP 1112494 A1 EP 1998-940489 19980908, WO 1998-IB1399 19980908; TW 429312 A TW 2000-102946 20000221; CN 1315001 A CN 1998-814290 19980908, WO 1998-IB1399 19980908; KR 2001106467 A WO 1998-IB1399 19980908, KR 2001-702960 20010307; US 2002081629 A1 Div ex WO 1998-IB1399 19980908, Div ex US 2000-530907 20000630, US 2001-25391 20011219

FDT AU 2000022512 A Based on WO 200014540; BR 9816009 A Based on WO 200014540; EP 1112494 A1 Based on WO 200014540

PRAI **WO 1998-IB1399 19980908; ZA 2000-891 20000223**

AN 2000-271085 [23] WPIX

AB WO 200014540 A UPAB: 20000516

NOVELTY - The analytes are simultaneously applied as spots (64) onto a solid support (61) in such a way that they remain isolated from one another. The support is contacted with targets in a semi-solid or liquid medium. Analytes are released from the support to the targets. Analyte-target interactions are measured.

DETAILED DESCRIPTION - The analytes are placed in individual identifiable containers, e.g. capillary tubes (41), pens or print heads, from where they are transferred to the solid support in such a way as to keep the contents of each container separate from those of all other containers. In the illustrated embodiment, the capillary tubes are held in an array (57), each tube identifiable according to its position in the array. The analytes are dispensed onto the solid support (61) through the open ends of the capillary tubes. The solid support is a flat, disc-, rectangular, or square-shape. The solid support is made of a material which allows for spontaneous or controlled release of the analytes. It may be semi-solid. When each analyte is applied, it diffuses on the support to produce a concentration gradient. The solid support may be a polymer, ceramic, metal, cellulose or glass. In another embodiment, the support is a flexible film or tape which is advanced through the various stages by a system of rollers. The solid support may be provided with a track for the recording of information. Thus information can be read and processed simultaneously with the measurement of analyte-target interactions in an automated process. The solid support may itself be the detector. The surface of the support may be coated with a membrane, a molecular monolayer, a cellular monolayer or a Langmuir-Blodgett film. The solid support may be the reflective surface of a compact disc. The target may be provided in a semi-solid or viscous liquid environment, e.g. gelatin, polysaccharides, or polymers such as methylcellulose and polyacrylamide, or a so-called intelligent material. The analytes may be chemical compounds, antigens, antibodies, DNA-probes, cells and beads and liposomes carrying an analyte of interest.

USE - Especially for the rapid screening of chemical compounds in liquid form for use as potential drugs.

ADVANTAGE - The apparatus can simultaneously handle large numbers of compounds in liquid form to provide high throughput screening.

DESCRIPTION OF DRAWING(S) - The figure illustrates a sample deposition pattern.

capillary tubes 41
array of capillary tubes 57

solid support 61
spots of analytes 64
Dwg.21/23

L49 ANSWER 77 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-246581 [21] WPIX
DNN N2000-184403 DNC C2000-074651
TI New compound for detecting an analyte comprising an acceptor and donor fluorophore, useful for detecting target molecules such as organic molecules e.g. pesticides, peptides and proteins and polysaccharides.
DC B04 C07 D16 **J04** K04 **S03**
IN LANNIGAN, D A; MACARA, I G
PA (UYVI-N) UNIV VIRGINIA PATENT FOUND
CYC 86
PI WO 2000011446 A2 20000302 (200021)* EN 22p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9954924 A 20000314 (200031) <--
US 6399302 B1 20020604 (200242) <--
ADT WO 2000011446 A2 WO 1999-US18904 19990820; AU 9954924 A AU 1999-54924 19990820; US 6399302 B1 Provisional US 1998-97478P 19980821, WO 1999-US18904 19990820, US 2000-529870 20000419
FDT AU 9954924 A Based on WO 200011446; US 6399302 B1 Based on WO 200011446
PRAI **US 1998-97478P 19980821; US 2000-529870 20000419**
AN 2000-246581 [21] WPIX
AB WO 200011446 A UPAB: 20000502
NOVELTY - A compound (I) for detecting an analyte is new and comprises an acceptor fluorophore and a donor fluorophore. The donor fluorophore has an emission spectrum that overlaps with the absorption spectrum of the acceptor fluorophore.

DETAILED DESCRIPTION - A compound for detecting an analyte is new and comprises the general formula (A): F1-A-L-B-F2

F1 and F2 = an acceptor fluorophore and a donor fluorophore respectively

A and B = ligands that independently bind to the analyte

L = a linking moiety

The donor fluorophore has an emission spectrum that overlaps with the absorption spectrum of the acceptor fluorophore.

INDEPENDENT CLAIMS are also included for the following:

(1) a compound (II) for detecting an analyte comprising the general formula (B): F1-X-A-L-B-Y-F2, where F1 and F2 are an acceptor fluorophore and a donor fluorophore respectively, A and B are ligands that independently bind to a non-nucleotide epitope, X and Y are complementary nucleic acid sequences and L is a linking moiety;

(2) a device for binding a preselected analyte comprising a solid matrix and a signal generating ligand complex covalently linked to the solid matrix and comprising the formula (A) or (B); and

(3) a method for detecting an analyte in a sample comprising:

(a) contacting one or more of (I) with the sample to form a detection mixture;

(b) exposing the detection mixture to a light source with a wavelength that is absorbed by the donor fluorophore but does not significantly overlap with the absorption spectrum of the acceptor fluorophore; and

(c) detecting the fluorescence from the detection mixture.

USE - (I) and (II) are used in assay methods, diagnostic procedures, cell sorting and other analytical procedures, including the use of (I) and (II) as probes. (I) and (II) are useful for the development of a target biosensor through the use of nucleic acid based, signal generating ligands

that can be used for detecting analytes. The biosensors are useful for detecting a wide variety of target molecules, such as small organic molecules (e.g. pesticides, herbicides, drugs, controlled substances, metabolites, explosives residues, plasticizers, industrial and agricultural pollutants, hormones), peptides and proteins (e.g. surface antigens on viruses, peptide hormones, cellular components), polysaccharides (e.g. surface antigens on bacteria and other pathogens) and other molecules.

ADVANTAGE - (I) and (II) comprise novel oligonucleotide aptamers which have an enhanced probability of undergoing a conformational change on binding to a target. The efficiency of resonance energy transfer varies with the sixth power of the separation between the donor and acceptor fluorophores and therefore provides a very sensitive readout. The detection complexes may not need to be specific to only one analyte, but rather a combination of detection complexes can be used to identify the presence of an analyte in a sample.

Dwg.0/0

TECH UPTX: 20000502

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Compounds: A and B are non-complementary nucleic acid sequences and L is a nucleic acid sequence that is covalently linked to A and B. (I) further comprises a tuning oligonucleotide comprising a nucleic acid sequence complementary to L. X and Y are 5-7 nucleotides in length.

L49 ANSWER 78 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-224719 [19] WPIX
DNC C2000-068780
TI Array for determining linkage of polymorphic forms in target nucleic acid and monitoring expression of mRNA population comprises support having three discrete regions, each containing pool of polynucleotide probes.
DC B04 D16
IN CHEE, M; GENTALEN, E
PA (AFFY-N) AFFYMETRIX INC
CYC 89
PI WO 2000011223 A1 20000302 (200019)* EN 53p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9955778 A 20000314 (200031) <--
EP 1108062 A1 20010620 (200135) EN <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 6306643 B1 20011023 (200165) <--
ADT WO 2000011223 A1 WO 1999-US19069 19990819; AU 9955778 A AU 1999-55778 19990819; EP 1108062 A1 EP 1999-942387 19990819, WO 1999-US19069 19990819; US 6306643 B1 US 1998-138958 19980824
FDT AU 9955778 A Based on WO 200011223; EP 1108062 A1 Based on WO 200011223
PRAI **US 1998-138958 19980824**
AN 2000-224719 [19] WPIX
AB WO 200011223 A UPAB: 20000419

NOVELTY - An array (A) comprising a support having three discrete regions, each containing a pool of polynucleotide probe(s), where the first region (R1) contains a probe (I), the second region (R2) contains a second probe (II) and the third region (R3) contains (I) and (II), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an array (B) comprising a support having R1-R3, where:

(a) R3 comprises (I) and (II) at a (I):(II) molar ratio (M1);

(b) R1 comprises (I) without (II) or with (II) present at a (I):(II) molar ratio (M2) greater than M1;

(c) R2 comprising (II) without (I) or (I) present at a (I):(II) molar ration (M3) less than M1;

(2) a method of determining linkage of polymorphic forms in a target nucleic acid comprising:

(a) hybridizing a diploid target nucleic acid having first and second polymorphic sites to (A); and

(b) determining a ratio of binding of the target nucleic acid to R3 and to R1 and R2 combined to indicate whether the polymorphic form of the first polymorphic site and the polymorphic form of the second polymorphic site are present in the same molecule of the diploid target nucleic acid;

(3) a method of sequencing a target nucleic acid comprising:

(a) hybridizing the target nucleic acid to (A) where (I) is complementary to a known marker;

(b) determining a sequence of a segment of the target nucleic acid from the relative binding of the target nucleic acid to the pools of probes; and

(c) mapping the position of the segment in the target sequence relative to the known marker;

(4) a method of monitoring expression of a mRNA population comprising:

(a) providing a sample comprising a population of mRNA molecules;

(b) hybridizing the population of mRNA molecules to (A) where (I) and (II) are complementary to nonoverlapping segments of a known mRNA molecule; and

(c) determining which discrete regions show specific binding to the population indicating which of the known mRNA molecules are present; and

(5) a method of analyzing a target nucleic acid:

(a) hybridizing a target nucleic acid to (A); and

(b) comparing binding of the target nucleic acid to R3 with the aggregate of the target nucleic acid binding to R1 and R2 to determine whether the target nucleic acid includes segments complementary to (I) and (II).

USE - The array and methods are useful for determining linkage of polymorphic forms in a target nucleic acid, sequencing a target nucleic acid, monitoring expression of a mRNA population or analyzing a target nucleic acid.

ADVANTAGE - Using pools of polynucleotide probes reduces the number of array cells required to analyze a given target sequence.

Dwg.0/7

TECH UPTX: 20000419

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Array: (I) and (II) are preferably, respectively, complementary to first and second nonoverlapping segments of a target sequence. The first and second nonoverlapping segments of the target sequence preferably, respectively, contain first and second polymorphic sites to which (I) and (II) are respectively complementary to. R1 preferably bears (I) with a third probe (III) and R2 preferably bears (II) with a fourth probe (IV), so R1, R2 and R3 comprise three pools of polynucleotide probes. The pools of probes preferably comprise first and second subsets, where in the first subset each pool has a common (I) and a different (II), and in the second subset, each pool has a common (I), different to that in the first subset, and a different (II).
Preparation: Arrays or probes can be synthesized in a step-by-step manner on a support or can be attached in presynthesized form. A preferred method of synthesis is VLSIPS (RTM) (Fodor et al., 1991, Fodor et al., 1993, Nature 364, 555-556; McGall et al., USSN 08/445,332; US 5,143854; EP 476,014), which entails the use of light to direct synthesis of oligonucleotide probes in high density.
The basic VLSIPS1 (RTM) approach can readily be adapted to synthesize pooled mixtures of probes. The component probes of a pool are synthesized in series. Synthesis of a pooled probes starts with a substrate covered with a photosensitive protective group. The group is partially removed by limited exposure of substrate to light. The deprotected sites are capped with a protective group that is nonphotosensitive but can be removed by

other means, such as a chemical solvent. The remaining sites are then exposed to more light removing the remaining photosensitive protective groups. Synthesis proceeds on the exposed sites in a step-by-step fashion until first members of pooled probes are synthesized. The nonphotosensitive capping groups are then removed. Synthesis proceeds anchored from these sites in a step-by-step fashion until second members of pooled probes are formed. After hybridization of control and target samples to an array containing one or more probe sets and optional washing to remove unbound and nonspecifically bound probe, the hybridization intensity for the respective samples is determined for each probe in the array. For fluorescent labels, hybridization intensity can be determined by, for example, a scanning confocal microscope in photon counting mode.

L49 ANSWER 79 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-160502 [14] WPIX
DNC C2000-050059
TI Analyzing nucleic acid sequences for detecting a mutation in the nucleic acid of interest.
DC A14 A89 B04 D16 **J04**
IN BOLES, T C; HAMMOND, P W
PA (MOSA-N) MOSAIC TECHNOLOGIES; (MOSA-N) MOSAIC TECHNOLOGIES INC
CYC 87
PI WO 9966078 A1 19991223 (200014)* EN 60p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9946898 A 20000105 (200024) <--
EP 1086248 A1 20010328 (200118) EN <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6214187 B1 20010410 (200122)
JP 2002518025 W 20020625 (200243) 44p <--
ADT WO 9966078 A1 WO 1999-US13649 19990618; AU 9946898 A AU 1999-46898 19990618; EP 1086248 A1 EP 1999-930343 19990618, WO 1999-US13649 19990618; US 6214187 B1 Provisional US 1998-89788P 19980618, US 1999-336228 19990618; JP 2002518025 W WO 1999-US13649 19990618, JP 2000-554885 19990618
FDT AU 9946898 A Based on WO 9966078; EP 1086248 A1 Based on WO 9966078; JP 2002518025 W Based on WO 9966078
PRAI **US 1998-89788P 19980618; US 1999-336228 19990618**
AN 2000-160502 [14] WPIX
AB WO 9966078 A UPAB: 20000320
NOVELTY - Analyzing nucleic acid sequences on an electrophoretic medium using a nucleic acid capture ligand immobilized in the medium and a spatial gradient of a nucleic acid denaturant is new.

DETAILED DESCRIPTION - (A) Analyzing the nucleic acid sequence of at least one target nucleic acid comprises:

(a) contacting the target nucleic acid with an electrophoretic medium comprising:

(i) at least one nucleic acid capture ligand immobilized in the medium, and

(ii) a spatial gradient of a nucleic acid denaturant;

(b) applying an electric field oriented in a direction parallel to the denaturant gradient under conditions wherein the target sample migrates from a region of high denaturant activity to a region of low denaturant activity and, where the target nucleic acid binds to the immobilized capture ligand at a position within the medium relative to the binding affinity between the target and capture ligand; and

(c) determining one of the following properties:

(i) the position of the target within the medium, or

(ii) the electrophoretic mobility of the target in the medium,

wherein the properties of the target determined in part (c) are dependent on the nucleotide sequence or structure of the target nucleic acid.

INDEPENDENT CLAIMS are included for the following:

(1) analyzing at least one target nucleic acid from other components in a test sample comprising:
(a) as in (Aa);
(b) as in (Ab);

(c) turning off the electric field after the target nucleic acids bind to the immobilized capture ligand;

(d) increasing the denaturant activity to a point wherein the target nucleic acids does not bind to the capture ligand;

(e) reapplying the electric field; and

(f) determining a time at which a target nucleic acid passes a position in the medium which is detected by a detector, detecting a position in the electrophoretic medium which is a greater distance, measured in the direction in which the target has migrated in step (b), from the position where the electrophoretic medium was contacted with the test sample than all of the target nucleic acid have migrated, thereby analyzing the target nucleic acid, and

(2) a kit for analyzing a target nucleic acid sequence of a test sample for the presence of at least one degenerate site comprising:

(a) an electrophoretic medium which comprises at least one capture ligand that is designed to type the degenerate site; and

(b) a means for creating a spatial gradient of a nucleic acid denaturant with in the electrophoretic medium.

USE - The methods can also be used in sequencing and mutation detection in the target nucleic acids.

Dwg.0/5

TECH UPTX: 20000320

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Methods: A property determined in part (c) is compared to the same property of a standard having a predetermined nucleic acid sequence. The method further comprises amplifying the target using an enzymatic amplification technique, especially polymerase chain reaction (PCR). At least one labeled deoxynucleotide triphosphate is used in the amplification technique. The target is detectably labeled. The target is directly labeled with a non-covalently bound detectable moiety. Alternatively, the target is indirectly labeled with a non-covalently bound detectable moiety. The method further comprises comparing the time for a target to reach the position detected by the detector to a time at which a standard nucleic acid reaches the position detected by the detector. The predetermined nucleic acid sequence of the standard is the same as at least one target. The electrophoretic medium is contained in a capillary electrophoresis apparatus. The electrophoretic medium is a slab gel.
Preferred Materials: The capture ligand is a modified nucleic acid or a nucleic acid analog, especially a peptide nucleic acid. The predetermined nucleic acid sequence of the standard is the same as the sequence of at least one target. The electrophoresis medium is polyacrylamide or its derivative, agarose or a soluble linear polymer. More than one nucleic acid capture ligand is immobilized throughout the electrophoresis medium. Alternatively, a single nucleic acid capture ligand, comprising more than one capture subsequence complementary to more that one region of the target, is immobilized throughout the electrophoresis medium. The denaturant is temperature or a chemical, especially urea or formamide.

L49 ANSWER 80 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-136998 [12] WPIX
DNN N2000-102412 DNC C2000-042044
TI Multi-sensor array for electrochemical recognition of nucleotide sequences especially for diagnosis of microorganism associated disease, especially bacterial, fungal and viral.
DC B04 D16 **J04** P85 **S03**
IN HARRISON, J I; HARRISON, M W; CARUANA, D J; DE LUMLEY-WOODYEAR, T; HELLER,

A
PA (HELL-N) HELLER & CO E; (THER-N) THERASENSE INC; (JOYM-N) JOYMAS INC
CYC 87
PI WO 9967628 A1 19991229 (200012)* EN 80p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT UA UG US UZ VN YU ZA ZW
US 6018117 A 20000125 (200012) <--
AU 9948338 A 20000110 (200025) <--
EP 1090286 A1 20010411 (200121) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 2002081588 A1 20020627 (200245) <--
JP 2002518998 W 20020702 (200246) 90p
ADT WO 9967628 A1 WO 1999-US14460 19990624; US 6018117 A US 1998-90517
19980604; AU 9948338 A AU 1999-48338 19990624; EP 1090286 A1 EP
1999-931928 19990624, WO 1999-US14460 19990624; US 2002081588 A1
Provisional US 1998-90517P 19980624, Provisional US 1998-93100P 19980716,
Provisional US 1999-114919P 19990105, Cont of WO 1999-US14460 19990624, US
2000-746620 20001221; JP 2002518998 W WO 1999-US14460 19990624, JP
2000-556236 19990624
FDT AU 9948338 A Based on WO 9967628; EP 1090286 A1 Based on WO 9967628; JP
2002518998 W Based on WO 9967628
PRAI **US 1999-114919P 19990105; US 1998-90517P 19980624**
; US 1998-93100P 19980716; US 1998-90517
19980604; US 2000-746620 20001221
AN 2000-136998 [12] WPIX
AB WO 9967628 A UPAB: 20000308

NOVELTY - A nucleic acid sensor (A) comprises:

(a) an electrode;

(b) a redox polymer disposed on the electrode; and

(c) an oligonucleotide probe coupled to the redox polymer.

The probe optionally comprises DNA, RNA (which can be ribosomal RNA). The sensor optionally comprises a catalyst, wherein the catalyst preferably is an enzyme, a thermostable enzyme, a peroxidase or a soybean peroxidase.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an array comprising (A)s disposed on a substrate, wherein each nucleic acid sensor comprises a particular oligonucleotide probe, wherein optionally at least two oligonucleotide probes comprise differing diagnostic sequences, and/or one or more of the probes optionally is diagnostic of a cancer, a disease and/or a pathogen;

(2) a method for producing a nucleic acid sensor, comprising:

(a) coating an electrode with a redox polymer;

(b) electrophoretically depositing an oligonucleotide onto the electrode and coupling the oligonucleotide to the redox polymer, wherein the electrophoretically depositing optionally comprises applying a potential to an electrode in the presence of the oligonucleotide, whereby the oligonucleotide selectively migrates to the electrode and binds to the redox polymer;

(3) a method for producing an array for the detection of nucleic acid sequence, comprising:

(a) depositing a plurality of electrodes on a substrate;

(b) coating the plurality of electrodes with a redox polymer; and

(c) selectively coupling an oligonucleotide probe to each electrode by electrophoretic deposition;

(4) a method for determining a nucleic acid sequence, comprising:

(a) contacting (A) with a sample nucleic acid sequence under conditions suitable for hybridization of the sequence to a complementary probe;

(b) correlating current generated at one or more electrodes with

hybridization of the sample sequence with the probe of the one or more electrode; and
(c) determining the nucleic acid sequence of the sample;
(5) a method for the diagnosis of disease, wherein the disease is a cancer, or a disease induced by a pathogen, comprising:
(a) applying a patient sample to a biosensor array, the array comprising a plurality of oligonucleotide sensors, each sensor comprising an electrode, a redox mediator disposed on said electrode; and a diagnostic oligonucleotide probe coupled to the redox mediator;
(b) reacting the sample and the array under conditions suitable for hybridization of the oligonucleotide probe and a complementary nucleic acid sequence; and
(c) correlating an electrochemical current generated at one or more electrodes of the array with hybridization of the sample to complementary oligonucleotide probes of the array diagnostic of disease, wherein the method optionally comprises adding a second oligonucleotide probe, the second oligonucleotide probe labeled with a catalyst, which may be an enzyme, designed to hybridize with the sample nucleic acid sequence hybridized on the array, wherein hybridization of the second oligonucleotide probe induces the transfer of an electrochemical signal from the catalyst to the electrode; and
(6) a diagnostic assay system comprising:
(a) an array comprising a plurality of electrically isolated sensors disposed on a substrate, each sensor comprising an electrode;
(b) a redox polymer disposed on the electrode; a first oligonucleotide probe coupled to the redox polymer; and
(c) a second oligonucleotide probe having attached thereto an enzyme, wherein the first and second oligonucleotide probes are designed to hybridize a specific target sequence, and wherein said enzyme induces an electrochemical signal upon hybridization of the first and second oligonucleotide probes to a target sequence.
USE - The microelectrode array is useful for the detection and recognition of low copy numbers of nucleic acid sequences for the diagnosis of diseases and for detecting microorganisms e.g. bacterial, fungal and eukaryotic pathogens. The electrode system may also be used for the simultaneous but multiple analysis and detection of nucleic acid sequences diagnostic of one or more particular diseases.
ADVANTAGE - The microelectrode array is suitable for efficient and rapid detection of low copy numbers of nucleic acid sequences. Te sensor arrays can be used without having to be amplified first as obtained from the tissue sample.
Dwg.0/17

TECH UPTX: 20000308
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred sensors: The density of sensors disposed on the substrate is at least 10-1000 sensors/cm2 and/or the electrode of each sensor has a dimension of at most 25 mum and/or each oligonucleotide comprises a sequence of at least 10-15 nucleotides.

L49 ANSWER 81 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-107926 [10] WPIX
CR 2000-655656 [58]
DNN N2000-083007 DNC C2000-032602
TI Verifying a manufacturing process useful for verifying the synthesis of polymers.
DC B04 D16 **J04** T01
IN HUBBELL, E A; SMITH, D P
PA (AFFY-N) AFFYMETRIX INC
CYC 28
PI EP 955085 A2 19991110 (200010)* EN 26p <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CA 2269846 A1 19991104 (200015) EN <--
JP 2000032998 A 20000202 (200017) 59p <--

US 6130046 A 20001010 (200063)# 23p <--
ADT EP 955085 A2 EP 1999-303194 19990426; CA 2269846 A1 CA 1999-2269846 19990422; JP 2000032998 A JP 1999-126422 19990506; US 6130046 A Provisional US 1998-98553P 19980504, US 1998-144514 19980831
PRAI **US 1998-144514 19980831; US 1998-72394 19980504**
AN 2000-107926 [10] WPIX
CR 2000-655656 [58]
AB EP 955085 A UPAB: 20001230

NOVELTY - A novel method of verifying a manufacturing process, comprising selecting two groups of steps from the process to produce verification objects, where the second verification object is the same as the first verification object, but the groups of steps differ by at least one step.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method of designing polymer probes, comprising providing a control sequence of monomers and designing polymer probes which have the same sequence of monomers and will bind with the control sequence, but are formed with at least one different monomer addition cycle, so that the polymer probe integrity may be verified;

(2) a computer program product which designs polymer probes, comprising computer codes which perform the method of (1) and a computer readable medium which stores the codes; and

(3) a substrate having polymer probes coupled to it, comprising regions on the substrate in which diverse probes are coupled, and regions on the substrate in which identical probes are coupled, the identical probes will bind with a control sequence of monomers but differ by one monomer addition cycle.

USE - The methods are used to verify the synthesis of polymers, which may be polymer probes, and to design polymer probes which have the same sequence but are formed with at least one different monomer addition cycle so that the integrity of the probes may be verified (claimed). An array of nucleic acid probes can be made at known locations on a chip, and can be contacted with a labeled nucleic acid. A scanner generates an image file indicating the location of the labeled nucleic acid. This allows the detection of the nucleotide monomer sequence of DNA or RNA molecules. This technique can be used study and detect mutations relevant to genetic diseases, cancers, infectious diseases, HIV, and other genetic characteristics.

ADVANTAGE - None given.

Dwg.0/14

TECH UPTX: 20000228

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Methods: The method of verifying a manufacturing process comprises first and second verification objects with the same structure. The verification objects are polymer probes, mechanical devices or electronic circuits. The method of designing polymer probes, preferably comprises determining a shortest path with a weighted directed acrylic graph to generate a list of monomer cycles for synthesizing a polymer probe, and utilizing a matrix to increase cycle differentiation. The polymer probes are represented as a list of monomer addition cycles. If the list of monomer cycles is undesirable, weights on the weighted directed acrylic graph are adjusted to prevent future undesirable lists. The polymer probes are attached to a substrate.
Preferred Computer Program: The computer readable medium is selected from the group consisting of floppy disk, tape, flash memory, system memory, hard drive, and a data signal embodied in a carrier wave.
Preferred Substrate: The regions are near the center of the substrate, preferably in a checkerboard pattern on the substrate.

L49 ANSWER 82 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-098630 [09] WPIX
DNN N2000-076054 DNC C2000-028888
TI Apparatus for nucleic acid assay by polymerase chain reaction.
DC A96 B04 D16 **S03**

IN BERTLING, W
PA (NOVE-N) NOVEMBER NOVUS MEDICATUS BERTLING GES MO; (NOVE-N) NOVEMBER GES MOLEKULARE MED AG; (BERT-I) BERTLING W; (NOVE-N) NOVEMBER GES MOLEKULARE MEDIZIN AG; (NOVE-N) NOVEMBER NOVUS MEDICULATUS BERTLING GES
CYC 22
PI DE 19826153 A1 19991216 (200009)* 11p <--
WO 9964157 A1 19991216 (200009) DE <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
EP 1096998 A1 20010509 (200128) DE
R: AT CH DE ES FR GB IT LI NL
US 2001010917 A1 20010802 (200147) <--
US 6383802 B1 20020507 (200235) <--
JP 2002517219 W 20020618 (200242) 34p
ADT DE 19826153 A1 DE 1998-19826153 19980612; WO 9964157 A1 WO 1999-DE1589 19990529; EP 1096998 A1 EP 1999-936358 19990529, WO 1999-DE1589 19990529; US 2001010917 A1 Div ex WO 1999-DE1589 19990529, Div ex US 2000-719376 20001211, US 2001-825826 20010404; US 6383802 B1 WO 1999-DE1589 19990529, US 2000-719376 20001211; JP 2002517219 W WO 1999-DE1589 19990529, JP 2000-553211 19990529
FDT EP 1096998 A1 Based on WO 9964157; US 6383802 B1 Based on WO 9964157; JP 2002517219 W Based on WO 9964157
PRAI **DE 1998-19826153 19980612**
AN 2000-098630 [09] WPIX
AB DE 19826153 A UPAB: 20000218

NOVELTY - Apparatus for detecting a target nucleotide sequence in a sample by polymerase chain reaction (PCR) comprises (a) a carrier with at least one well for receiving an assay solution, (b) a lid with a shape complementary to the well, which can be placed onto the carrier so that the assay solution is at least partly displaced into a gap between the well and the lid, and (c) seals in the vicinity of the well opening for sealing the gap.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method detecting a target nucleotide sequence in a sample by polymerase chain reaction in which an assay solution is introduced into the well and the lid is placed onto the carrier so that the assay solution is at least partly displaced into the gap between the well and the lid.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - For detecting target nucleic acid sequences in liquid samples.

ADVANTAGE - Laborious filling and sealing of glass capillaries is avoided (compare US5455175).

DESCRIPTION OF DRAWING(S) - The figure shows a schematic cross-sectional view of an apparatus with first seals between the wells and the corresponding lid projections and second seals between adjacent wells.

Carrier 1
Lis 2
First seals 5
Second seals. 12
Dwg.3/6

TECH UPTX: 20000218

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The assay solution contains two primers, and a third primer is attached at its 5' end to the inside of the lid to capture the target sequence so that it is enriched on the lid after the amplification cycles, preferably under the influence of an electric field. The assay solution and/or primer(s) are assayed for fluorescence, especially a change in fluorescence due to a change in the spatial relationship between two fluorophores. The assay solution is cyclically heated and cooled. Heating is effected with infrared radiation, by resistance heating or by contacting the wells with a hot gas or liquid stream. Cooling is effected by contacting the wells with a cold gas or liquid stream or by means of a Peltier element. Preferred Apparatus: The

carrier is made of transparent material, e.g. glass or plastic. The well is in the form of an inverted cone with a flat base. Seals are located between adjacent wells in the carrier or between corresponding projections of the lid. The carrier has 96 wells and the lid has 96 complementary projections. The lid is made of electrically conductive material, preferably a plastic, especially a polycarbonate, trimethylthiophene (sic), triaminobenzene (sic) or polycarbene, and its inside is at least partly coated with a biomolecule-binding substance. The carrier is provided with an electrode, preferably of platinum, so that an electric field can be applied to cause the target nucleotide sequence to migrate towards the inside of the lid and be enriched by field inversion cycles. The apparatus also includes a laser diode whose radiation can be focussed on the inside of the lid, a device for detecting the resulting fluorescence, and a device for moving the carrier relative to the laser diode and/or the detection device. At least part of the lid and/or carrier is colored black to absorb radiated heat. The seal between the well and complementary lid projection is formed by a circumferential bead on the projection fitting into a corresponding groove in the well.

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Apparatus: The carrier is made of transparent material, e.g. glass or plastic. The well is in the form of an inverted cone with a flat base. Seals are located between adjacent wells in the carrier or between corresponding projections of the lid. The carrier has 96 wells and the lid has 96 complementary projections. The lid is made of electrically conductive material, preferably a plastic, especially a polycarbonate, trimethylthiophene (sic), triaminobenzene (sic) or polycarbene, and its inside is at least partly coated with a biomolecule-binding substance. The carrier is provided with an electrode, preferably of platinum, so that an electric field can be applied to cause the target nucleotide sequence to migrate towards the inside of the lid and be enriched by field inversion cycles. The apparatus also includes a laser diode whose radiation can be focussed on the inside of the lid, a device for detecting the resulting fluorescence, and a device for moving the carrier relative to the laser diode and/or the detection device. At least part of the lid and/or carrier is colored black to absorb radiated heat. The seal between the well and complementary lid projection is formed by a circumferential bead on the projection fitting into a corresponding groove in the well.

L49 ANSWER 83 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 2000-072188 [06] WPIX
DNC C2000-020557
TI Formation of peptide nucleic acid probe triplexes for detection, quantitation and analysis of nucleic acid target sequences.
DC B04 D16 **J04**
IN COULL, J; HYLDIG-NIELSEN, J J; PETERSEN, K H; STEFANO, K; STENDER, H; COULL, J M; PETERSON, K H
PA (BOST-N) BOSTON PROBES INC; (DAKO-N) DAKO AS
CYC 23
PI WO 9955916 A1 19991104 (200006)* EN 83p <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 9937750 A 19991116 (200015) <--
EP 1073767 A1 20010207 (200109) EN <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6287772 B1 20010911 (200154) <--
US 2002058278 A1 20020516 (200237) <--
ADT WO 9955916 A1 WO 1999-US9433 19990429; AU 9937750 A AU 1999-37750 19990429; EP 1073767 A1 EP 1999-920194 19990429, WO 1999-US9433 19990429; US 6287772 B1 Provisional US 1998-83649P 19980429, US 1999-302238 19990429; US 2002058278 A1 Provisional US 1998-83649P 19980429, Cont of US 1999-302238 19990429, US 2001-950255 20010910
FDT AU 9937750 A Based on WO 9955916; EP 1073767 A1 Based on WO 9955916; US

2002058278 A1 Cont of US 6287772
PRAI **US 1998-83649P 19980429; US 1998-70546 19980429**
; US 1999-302238 19990429; US 2001-950255 20010910
AN 2000-072188 [06] WPIX
AB WO 9955916 A UPAB: 20000203
NOVELTY - A peptide nucleic acid (PNA) probe triplex is formed by contacting a sample containing a target nucleic acid under hybridization conditions to at least one probe set comprising three probes where the first and second probes comprise a probing segment and a PNA arm segment and where the third probe comprises a PNA arm segment.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method for detecting the presence or quantity of target nucleic acid present in a sample, comprising detecting the presence or quantity of a PNA probe triplex, where the presence or quantity of the PNA probe triplex is indicative of the presence or quantity of target nucleic acid in the sample;

(2) a probe set comprising first, second and third probes as above;

(3) a probe triplex/target nucleic acid complex; and

(4) a kit suitable for detecting the presence or amount of target nucleic acid in a sample.

USE - The methods, kits and probes are suitable for the improved detection, quantitation and analysis of nucleic acid target sequences using probe-based hybridization assays.

ADVANTAGE - The three component polymers and the target nucleic acid interact in order to produce a detectable signal, even in the presence of non-target sequences. The methods, etc. improve the specificity and sensitivity of the assay thereby improving the signal to noise ratio of the assay. The PNA triplex structures exploit the advantages of using short probes as a means to achieve specificity while still possessing the sequence diversity associated with longer probes. Additionally, the PNA probe triplexes can be designed without regard to treatment considerations for the orientation of probes within the triplex.
Dwg.0/11
TECH UPTX: 20000203
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The arm segments of the first and second probes do not hybridize to each other. The PNA arm segments of the first and second probes comprise a polypyrimidine nucleobase sequence. The PNA arm of the third probe comprises a polypurine nucleobase sequence. The probing segment of the first or second probes has a length of about 5-25 nucleobases. The arm segment of the first, second and third probes has a length from about 2-16 nucleobases. The probing segments of the first and second probes are chosen from PNA, ribonucleic acid, deoxyribonucleic acid, chimeric oligomer and linked polymer. The probing and arm segments are joined by a linker. The arm segment of the third probe orients in an antiparallel manner with respect to the arm segment of the first, second or both first and second probes. The target nucleic acid is of human origin and is specific for a genetically based disease or a predisposition for it. The target nucleic acid is immobilized to a support. The first and second sites of hybridization are on the same nucleic acid strand and are separated by 5 or fewer nucleotides. Alternatively the first and second sites of hybridization exist on complementary strands of a double stranded target nucleic acid. At least two probe sets are used. The probing segments of the first and second probes of each probe set are variable and in combination each set hybridizes to a unique target nucleic acid sequence and the PNA arm segments of the first, second and third probes are variable and form a different PNA probe triplex structure depending on which unique target nucleic acids are present in the sample. Alternatively, the PNA arm segments of the first, second and third probes of all probe sets are constant and form the same PNA probe triplex regardless of the nature of the unique target nucleic acid to which it is bound. At least one of the first or second probes or third probe is immobilized to a solid carrier. The method further comprises separating the solid carrier from the sample

and optionally recovering or detecting the target nucleic acid. At least one of the other probes of the set is labeled with a detectable moiety.

L49 ANSWER 84 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 1999-590979 [50] WPIX
DNC C1999-172495
TI Analyzing differences in nucleic acid sequences.
DC B04 D16 **J04**
IN REEVE, M A; SCHWARZ, T
PA (AMSH) NYCOMED AMERSHAM PLC; (AMSH) AMERSHAM BIOSCIENCES UK LTD
CYC 87
PI WO 9947706 A1 19990923 (199950)* EN 22p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9929486 A 19991011 (200008) <--
EP 1071814 A1 20010131 (200108) EN <--
R: BE CH DE DK FR GB IT LI NL SE
JP 2002509701 W 20020402 (200225) 23p <--
US 6399364 B1 20020604 (200242) <--
ADT WO 9947706 A1 WO 1999-GB875 19990319; AU 9929486 A AU 1999-29486 19990319; EP 1071814 A1 EP 1999-910560 19990319, WO 1999-GB875 19990319; JP 2002509701 W WO 1999-GB875 19990319, JP 2000-536888 19990319; US 6399364 B1 WO 1999-GB875 19990319, US 2000-646530 20001109
FDT AU 9929486 A Based on WO 9947706; EP 1071814 A1 Based on WO 9947706; JP 2002509701 W Based on WO 9947706; US 6399364 B1 Based on WO 9947706
PRAI **GB 1998-5918 19980319**
AN 1999-590979 [50] WPIX
AB WO 9947706 A UPAB: 19991201
NOVELTY - A method for analyzing a target nucleic acid using a mixture of labeled oligonucleotides in solution and an array of immobilized oligonucleotides, in new.

DETAILED DESCRIPTION - The method comprises:

(i) incubating under hybridization conditions the target and mixture;

(ii) recovering those labeled oligonucleotides that hybridized with the target;

(iii) incubating the recovered oligonucleotides from (ii) with the array of immobilized oligonucleotides; and

(iv) observing the distribution of the labeled oligonucleotides on the array and using the information to analyze the target nucleic acid.

INDEPENDENT CLAIMS are also included for the following:

(1) a method of determining differences between a target nucleic acid and a reference nucleic acid, using two oligonucleotide mixtures with different labels, and an array of immobilized oligonucleotides, comprising:

(a) incubating the target nucleic acid the first mixture under hybridization conditions, and incubating the reference nucleic acid with the second set of oligonucleotides;

(b) recovering the oligonucleotides that bind their corresponding nucleic acid;

(c) incubating the re covered oligonucleotides with the array of immobilized oligonucleotides; and

(d) observing the distribution of labeled oligonucleotides, and so determining differences between the target and reference nucleic acids; and

(2) a kit for performing the above methods, comprising the labeled oligonucleotides in solution, and an array of immobilized oligonucleotides.

USE - The methods are useful for determining differences between target and reference nucleic acids (claimed).

ADVANTAGE - Nucleotide analogues may be used in the invention, preventing problems in PCR due to secondary structures. All hybridization events are internally controlled for absolute hybridization intensities. The method does not use enzymes, therefore is more robust and reliable than the prior art. A single array of all possible N-mers or subset can be employed for the analysis of any nucleic acid system. The optimal size of prior art systems is 200 bp, compared to 1-10 kb fragments in the new method.
Dwg.0/0

TECH UPTX: 19991201
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The target and reference nucleic acid in (i) are immobilized. The labeled oligonucleotides in (i) are a complete set or a subset of all N-mers where N is 5-10, preferably 8 or 9. The labeled oligonucleotides and array oligonucleotides are DNA, RNA, PNA or other nucleic acid mimetics or mixtures, and are single or partially double stranded, and may contain nucleotide analogue(s). Target nucleic acid is generated by PCR.

L49 ANSWER 85 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 1999-541580 [46] WPIX
DNN N1999-401430 DNC C1999-158359
TI Identifying marker that indicates presence of immobilized nucleic acid using fluorophore-labeled detection agent bound to solid phase.
DC B04 D16 **J04 S03**
IN BERTLING, W
PA (NOVE-N) NOVEMBER NOVUS MEDICATUS BERTLING GES MO; (NOVE-N) NOVEMBER GES MOLEKULARE MED AG
CYC 22
PI DE 19811730 A1 19990923 (199946)* 13p <--
WO 9947702 A2 19990923 (199947) DE <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
EP 1064409 A2 20010103 (200102) DE <--
R: AT BE CH DE DK ES FR GB IT LI NL
JP 2002506656 W 20020305 (200220) 35p <--
ADT DE 19811730 A1 DE 1998-19811730 19980318; WO 9947702 A2 WO 1999-DE729 19990316; EP 1064409 A2 EP 1999-920549 19990316, WO 1999-DE729 19990316; JP 2002506656 W WO 1999-DE729 19990316, JP 2000-536885 19990316
FDT EP 1064409 A2 Based on WO 9947702; JP 2002506656 W Based on WO 9947702
PRAI **DE 1998-19811730 19980318**
AN 1999-541580 [46] WPIX
AB DE 19811730 A UPAB: 20011203
NOVELTY - A method for identifying a marker that indicates presence of a first nucleotide sequence (3), on a solid object (1), is new and comprises contacting (3) with a detection agent that includes a nucleotide sequence (5) complementary to (3). (5) is bound at one end to a solid phase (D) and at the other end to a fluorophore (6).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a device for carrying out the process.

USE - The method is used to detect specific nucleic acid sequences.

ADVANTAGE - The marker is identified simply and quickly, without the need to prepare solutions.

DESCRIPTION OF DRAWING(S) - The diagram shows hybridization in the presence of a magnetic field where a fluorophore (6) can be detected since it is no longer close to quencher (8). Hybridization between the target sequence (3) and its complement (5) is disrupted when the magnetic field is turned off, causing the magnetic bead (4) to fall back to support (1), and allowing rehybridization of (5) and (7), resulting in quenching of fluorescence.
Dwg.5/10

TECH UPTX: 19991110
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Fluorophores: The acceptors are (6-carboxy)tetramethylrhodamine or fluorescein. The donors

are e.g. (6-carboxy)fluorescein, and the quencher is 4-(4'-dimethylaminophenylazo) benzoic acid.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Contact between (3) and (5) involves hybridization and before, or during, contact, hybridization between (3) and a third sequence may be disrupted. Hybridization of (3) and (5) results in a fluorescent reaction and during contact (3) may be moved towards (5) by application of a magnetic field. Before contact, the marker is heated to above 50degreesC and afterwards cooled to below 50degreesC. Hybridization between (3) and (5) is assisted by light at a predetermined wavelength.
Preferred Apparatus: One end of (3) is attached covalently, to (1), via a spacer (2), while the other end is attached to a magnetic material (4), in which case the detection system includes a magnet. The detection system may also include a third nucleotide sequence (7), at least a segment of which is complementary to (3) and (5). (7) is linked at one end to D, via a spacer, and at the other end to a second fluorophore or quencher. When (5) and (7) are hybridized, an interaction between the fluorophores (one of which may be replaced by a quencher) is created or destroyed. The detection system also includes a light source and/or fluorescent detector. The surface of D is particularly coated with a layer of water-retentive material, e.g. poly(ethylene glycol) or glycerol.
Preferred Materials: All nucleic acids are DNA or peptide nucleic acids. The magnetic agent is a magnetic plastic or iron oxide particle, particularly of 20-200 nm. The solid phase D is of light-transmitting material, e.g. plastic, glass or quartz.

L49 ANSWER 86 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 1999-406140 [35] WPIX
DNC C1999-120181
TI Analyzing cell contents, especially nucleic acids, useful for medical diagnostics.
DC B04 D16
IN DOBLER, H; GUETH, A; KIESEWETTER, S; LINDNER, H; MICHNIEWSKI, M; SCHUELE, A; VOHRER, U
PA (FRAU) FRAUNHOFER GES FOERDERUNG ANGEWANDTEN
CYC 1
PI DE 19801730 A1 19990722 (199935)* 9p <--
ADT DE 19801730 A1 DE 1998-19801730 19980119
PRAI **DE 1998-19801730 19980119**
AN 1999-406140 [35] WPIX
AB DE 19801730 A UPAB: 20011203
NOVELTY - A process for the analysis of cell contents, especially nucleic acids, uses a substrate specific for the cell component being analyzed bound to macroscopic particles, and ultrasound energy, to produce an analyte with is then subjected to PCR analysis.

DETAILED DESCRIPTION - The new process comprises:

(1) adding macroscopic particles comprising a cell content-specific substrate on their surface to a buffered cell solution;

(2) lyzing the cells and isolating of the cell contents using ultrasound energy;

(3) separation and washing of the macroscopic particle-bound cell contents from the buffer solution within the reaction vessel; and

(4) drying of the complexes; and

(5) amplification and detection of the cell contents using polymerase chain reaction (PCR).

An INDEPENDENT CLAIM is also included for a device for carrying out the method described above.

USE - The process is used in medical diagnostics.

DESCRIPTION OF DRAWING(S) - reaction vessel 1
cell sample 2
buffer solution 3
macroscopic particles 4

ultrasound energy 5
amplification reagents 6
detection reagents 7
light source 8
vessel resonator 9
cooling medium 10
ultrasound source 11
separation device 12
septum 13
sample volume 14
cells 15
DNA binding substance 16
ultrasound resonator 17
nucleic acids 18
cell fragments 19
release valve 20
.
Dwg.3/5

TECH UPTX: 19990902
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Materials: The macroscopic particles are glass beads treated with substances with affinity fro DNA. The buffer solution comprises 100 mM potassium- or sodium phosphate, 3 M sodium chloride and pH 5-8. The cell suspension comprises 102-109 cells. The reaction vessel is connected to an ultrasound source which may be heated or cooled and which emits sound waves of 10-30 kHz into the cell suspension. The reaction vessel also comprises filtration devices to retain the unwanted cell contents. The washing step is carried out with water or buffer to free any impurities from the DNA-particle complexes. The cell extracts are washed up to 3 times and the wash solution is decanted or pipetted off. The DNA-particle complexes are dried in an air stream. For the amplification of the DNA, a PCR probe-containing buffer with marker molecules is added to the reaction vessel. The marker molecules are fluorescent. A fluorescence detector is used for the detection of the amplified DNA.
Preferred Method: The reaction vessel is cooled and heated during the amplification process.

L49 ANSWER 87 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 1999-156548 [14] WPIX
DNN N1999-113192 DNC C1999-046295
TI New de-oxy-ribose nucleic acid (DNA) probe analyser - provided with incubator for heat retention at process temperature.
DC B04 D16 **S03**
IN ARAI, T; NAKAJIMA, T; OKUMOTO, K; UEMATSU, H
PA (FURE) FURUNO DENKI KK; (TOYM) TOYOBO KK; (FURE) FURUNO ELECTRIC CO LTD; (TOYM) TOYO BOSEKI KK
CYC 2
PI JP 11009259 A 19990119 (199914)* JA 10p <--
US 6146882 A 20001114 (200060) <--
ADT JP 11009259 A JP 1997-163724 19970620; US 6146882 A WO 1998-JP2658 19980615, US 1999-242448 19990330
PRAI **JP 1997-163724 19970620**
AN 1999-156548 [14] WPIX
AB JP 11009259 A UPAB: 19990412
NOVELTY - An incubator retains the arbitrary process temperature and stores the well rack containing test samples. Cooling temperature is set by a cooler. A dummy rack is cooled by the cooler during heat retention process and an exchange unit is provided to exchange the well rack with dummy rack.

USE - The probe analyser is useful for analysing DNA extracted from blood.

ADVANTAGE - The method enables heat retention in the rack containing test samples.

Dwg.1/9

L49 ANSWER 88 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 1999-142965 [12] WPIX
DNC C1999-041894
TI Manipulating nucleic acids in arrays - by carrying out reactions such as amplification at the dew point to prevent evaporation and prevent spreading and merging of reactions.
DC A96 B04 D16
IN MOYNIHAN, K; TABONE, J C; VAN NESS, J; NESS, J V
PA (QIAG-N) QIAGEN GENOMICS INC; (RAPI-N) RAPIGENE INC; (MOYN-I) MOYNIHAN K; (NESS-I) NESS J V; (TABO-I) TABONE J C
CYC 79
PI WO 9905321 A1 19990204 (199912)* EN 50p <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU
AU 9885032 A 19990216 (199926) <--
EP 1000175 A1 20000517 (200028) EN <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1265156 A 20000830 (200059) <--
HU 2000002356 A2 20001128 (200103) <--
AU 729134 B 20010125 (200111) <--
US 6248521 B1 20010619 (200137) <--
JP 2001511361 W 20010814 (200154) 55p <--
NZ 501917 A 20011026 (200176) <--
US 2002037510 A1 20020328 (200225) <--
ADT WO 9905321 A1 WO 1998-US15042 19980721; AU 9885032 A AU 1998-85032 19980721; EP 1000175 A1 EP 1998-935866 19980721, WO 1998-US15042 19980721; CN 1265156 A CN 1998-807483 19980721; HU 2000002356 A2 WO 1998-US15042 19980721, HU 2000-2356 19980721; AU 729134 B AU 1998-85032 19980721; US 6248521 B1 Provisional US 1997-53428P 19970722, US 1998-120501 19980721; JP 2001511361 W WO 1998-US15042 19980721, JP 2000-504288 19980721; NZ 501917 A NZ 1998-501917 19980721, WO 1998-US15042 19980721; US 2002037510 A1 Provisional US 1997-53428P 19970722, Div ex US 1998-120501 19980721, US 2001-785105 20010214
FDT AU 9885032 A Based on WO 9905321; EP 1000175 A1 Based on WO 9905321; HU 2000002356 A2 Based on WO 9905321; AU 729134 B Previous Publ. AU 9885032, Based on WO 9905321; JP 2001511361 W Based on WO 9905321; NZ 501917 A Based on WO 9905321; US 2002037510 A1 Div ex US 6248521
PRAI **US 1997-53428P 19970722; US 1998-120501 19980721**
; US 2001-785105 20010214
AN 1999-142965 [12] WPIX
AB WO 9905321 A UPAB: 19990324
The following are claimed: (1) amplifying nucleic acid molecules (NAMs) from a template by: (a) mixing single-stranded (ss) nucleic acid templates on a solid **substrate** with a solution comprising an oligonucleotide (ON) primer that hybridises to the templates and a DNA polymerase, where the mixing occurs in discrete areas on the **substrate** and where the solution remains in the discrete areas; (b) synthesising a complementary strand to the template to form a duplex; (c) denaturing the duplex, and (d) synthesising complementary strands to the template, and amplifying the NAMs, where mixing, synthesising, and denaturing are conducted at dew point; (2) amplifying NAM's from a template by: (a) mixing ss nucleic acid templates on a solid **substrate** with a solution comprising two ON primers that hybridise to the respective templates, and is as in (1a), and (b) as in (1b)-(1d); (3) synthesising a NAM from a template by: (a) mixing ss nucleic acid templates on a solid **substrate** with a solution comprising an ON primer that hybridises to the templates and is as in (1a), and (b) synthesising a complementary strand to the template to form a duplex,

where mixing and synthesis are performed at dew point, where dew point is achieved by an apparatus comprising a container capable of being pressurised, a heating device, a device for generating pressure and a device for generating saturated steam, which are all controllable; (4) detecting a single base alteration in a NAM comprising: (a) mixing ss NAMs on a solid **substrate** with a solution comprising a first and a second ONs that hybridise to the NAMs and a DNA ligase, where the mixing occurs in a discrete area of an array, and where the solution remains in the discrete areas; and (b) detecting a ligation product; where (i) the first and second ONs will not ligate when there is a single base alteration at the junction base on the NAM; (ii) mixing is performed at dew point; and (iii) dew point is achieved by an apparatus comprising a container capable of being pressurised, a heating device, a device for generating pressure and a device for generating steam which are all controllable; (5) performing single nucleotide extension assay by: (a) mixing ONs on a solid **substrate** with a solution comprising ss NAMs that hybridise to the ONs a single nucleotide, and a DNA polymerase, where the mixing occurs in discrete areas of the **substrate**, and where the solution remains in discrete areas; and (b) detecting an extension product of the ON where: (i) the ON will be extended only when the single nucleotide is complementary to the nucleotide adjacent to the hybridised ON; (ii) mixing is performed at dew point; and (iii) dew point is achieved by an apparatus comprising a container capable of being pressurised, a heating device, a device for generating pressure, and a device for generating saturated steam, which are all controllable; (6) a kit for genotyping comprising a solid **substrate** containing an array of labelled ON primer pairs; (7) an instrument for maintaining a chamber at dew point during temperature cycling in the range of about 4 deg. C to 95 deg. C comprising: (a) a heating and cooling block; (b) an airtight chamber capable of covering the block; (c) a device for adjusting the pressure in the chamber; and (d) a device for injecting water vapour into the chamber; and (8) an instrument for maintaining a chamber at dew point during temperature cycling in the range of 4 deg. C to 95 deg. C comprising: (a) an airtight chamber capable of covering a heating and cooling block; (b) a seal between the chamber and the block; (c) a device for adjusting the pressure in the chamber; and (d) a device for injecting water vapour into the chamber.

USE - The methods can be used for amplifying, synthesising and analysing NAMs. They can be used for genotyping individuals, for mutation scanning, for determining expression profiles and for detection of nucleic acids to identify e.g. viruses or microorganisms.

ADVANTAGE - By carrying out reactions at the due point, evaporation during heating and cooling cycles can be prevented and spreading and merging of the reactions on the array can be prevented.

Dwg.0/5

L49 ANSWER 89 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 1999-081095 [07] WPIX
DNN N1999-058283 DNC C1999-024409
TI Deposition of compounds on solid **substrates** - by electrospraying a solution of a non-volatile biologically functional or biologically active substances on a surface of the **substrate**.
DC B04 D16 **J04** P42 **S03**
IN MOROZOV, V N; MOROZOVA, T Y; MOROZOV, V
PA (UYNY) UNIV NEW YORK STATE
CYC 24
PI WO 9858745 A1 19981230 (199907)* EN 111p <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP NZ US
AU 9880743 A 19990104 (199921) <--
EP 988112 A1 20000329 (200020) EN <--
R: AT BE CH DE FR GB LI SE
US 6350609 B1 20020226 (200220) <--

US 2002048770 A1 20020425 (200233) <--
AU 747022 B 20020509 (200238)
JP 2002511792 W 20020416 (200242) 104p

ADT WO 9858745 A1 WO 1998-US12768 19980619; AU 9880743 A AU 1998-80743 19980619; EP 988112 A1 EP 1998-929102 19980619, WO 1998-US12768 19980619; US 6350609 B1 Provisional US 1997-50274P 19970620, Provisional US 1997-55287P 19970813, WO 1998-US12768 19980619, US 2000-446188 20000508; US 2002048770 A1 Provisional US 1997-50274P 19970620, Provisional US 1997-55287P 19970813, Div ex WO 1998-US12768 19980619, Div ex US 2000-446188 20000508, US 2001-986334 20011108; AU 747022 B AU 1998-80743 19980619; JP 2002511792 W WO 1998-US12768 19980619, JP 1999-504841 19980619

FDT AU 9880743 A Based on WO 9858745; EP 988112 A1 Based on WO 9858745; US 6350609 B1 Based on WO 9858745; AU 747022 B Previous Publ. AU 9880743, Based on WO 9858745; JP 2002511792 W Based on WO 9858745

PRAI **US 1997-55287P 19970813; US 1997-50274P 19970620 ; US 2000-446188 20000508**; US 2001-986334 20011108

AN 1999-081095 [07] WPIX

AB WO 9858745 A UPAB: 19990302

A method is claimed for fabricating a deposit of a non-volatile biologically functional (BF) and/or biologically active (BA) substance on a **substrate**, comprising electrospraying a solution of the BF and/or BA substance on a surface of the **substrate**. Also claimed are: (1) a protein film formed on a **substrate** by electrospraying a solution of a protein, where the protein film has a thickness within a range from 0.4 to 20 microns, and has a homogeneity of thickness not larger than plus or minus 10%; (2) a sample comprising a **substrate** , and electrosprayed deposits of different BF and/or BA substances on the **substrate**, where each deposit has a size at most 7 microns; (3) an apparatus for depositing a sample of a non-volatile BF and/or BA substance onto a deposit area of a **substrate** by electrospraying a solution comprising a non-volatile BF and/or BA substance; the apparatus comprising: (a) an electrosprayer for creating from the solution, in a gas-filled space, a mist of charged particles including the non-volatile BF and/or BA substance; (b) an electrophotic device for creating, selectively by illumination or non-illumination; a first potential, attractive to the charged particles, on the deposit areas of the **substrate** surface; and a second potential, not attractive to the charged particles, on areas of the **substrate** surface other than the deposit areas; (4) an apparatus for depositing a sample of a non-volatile BF and/or BA substance onto a deposit area of a **substrate** by electrospraying a solution comprising a non-volatile BF and/or BA substance, the apparatus comprising: (a) an electrosprayer for creating from the solution, in a gas-filled space, a mist of charged particles including the non-volatile BF and/or BA substance; (b) a first electrostatic device holding a surface of the **substrate** adjacent to the deposit area at a first potential attractive to the charged particles; and (c) a mask held at a potential repulsive to the charged particles, the mask being disposed a distance above the surface of the **substrate**, the mask including a hole located above the deposit area; where a size of the hole is in a predetermined ratio to the distance, and where the predetermined ratio, the first potential, and the second potential generate an electric field in a region of the hole whereby the charged particles are focused and the deposit area is smaller than a hole area of the hole.

USE - The methods can be used for the deposition of biological molecules such as proteins and DNA or organic or inorganic molecules into a specified shape or pattern over a **substrate** surface. They can be used for preparing multicomponent chips. The multicomponent chips can be used as replaceable sensitive elements of chemo-sensors, in multianalyte assays, such as microELISA, nucleic acid hybridisation analysis, or in screening for effective enzyme inhibitors. Macro-chips can be used to prepare diagnostic tests for sensitivity to allergens, or for

analysis of microbial sensitivity to antibiotics.
ADVANTAGE - The electrospraying method can provide for the rapid, efficient deposition of biomolecules while retaining the activities of the biomolecules.
Dwg.0/34

L49 ANSWER 90 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 1998-559447 [48] WPIX
CR 2002-438026 [47]
DNC C1998-167627
TI Automated nucleic acid hybridisation assay - used to detect e.g. Mycobacterium tuberculosis, Chlamydia trachomatis, Neisseria gonorrhoeae and HIV.
DC B04 D16
IN BURG, J L; CATANZARITI, L; KLUTTZ, B W; MCKINLEY, G A; MOE, J G; VERA-GARCIA, M; BURG, L J; CATANZARIT, L; GARCIA, M V
PA (INMR) BIOMERIEUX VITEK INC
CYC 32
PI EP 875584 A2 19981104 (199848)* EN 60p <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
AU 9863766 A 19981105 (199905) <--
JP 10304890 A 19981117 (199905) 38p <--
CA 2230967 A 19981102 (199915) <--
BR 9801572 A 19990629 (199937) <--
KR 98086701 A 19981205 (200009) <--
MX 9803500 A1 19990201 (200055) <--
US 6300068 B1 20011009 (200162) <--
AU 2001058009 A 20011018 (200174)# <--
ADT EP 875584 A2 EP 1998-303458 19980501; AU 9863766 A AU 1998-63766 19980501; JP 10304890 A JP 1998-123564 19980506; CA 2230967 A CA 1998-2230967 19980501; BR 9801572 A BR 1998-1572 19980504; KR 98086701 A KR 1998-15754 19980501; MX 9803500 A1 MX 1998-3500 19980430; US 6300068 B1 Div ex US 1997-850171 19970502, US 1999-245939 19990205; AU 2001058009 A Div ex AU 1998-63766 19980501, AU 2001-58009 20010814
PRAI **US 1997-850171 19970502; US 1999-245939 19990205**
; AU 2001-58009 20010814
AN 1998-559447 [48] WPIX
CR 2002-438026 [47]
AB EP 875584 A UPAB: 20020725
A unified buffer for an isothermal amplification assay for denaturation of double-stranded nucleic acids and for annealing of nucleic acids, which is further capable of sustaining the activity of a nucleic acid polymerisation enzyme, comprising a sample dilution buffer, amplification reconstitution buffer and enzyme dilution buffer, is new. Also claimed are: (i) generation of a universal positive amplification internal control nucleic acid, comprising generating random nucleic acid sequences of at least ten nucleotides in length, screening them and selecting for specific functionality, combining in tandem more than one such selected nucleic acid, screening the combined nucleic acid sequences and optionally selecting against formation of intra-strand nucleic acid dimers or formation of hairpin structures; (ii) a universal positive amplification internal control nucleic acid sequence comprising a nucleic acid sequence which is randomly generated; (iii) detection of the presence or absence of a single-stranded or double-stranded first nucleic acid in a sample by automated isothermal amplification of the first nucleic acid in a dual chamber reaction vessel comprising first and second reaction chambers, which may be placed in fluid communication with each other such that the fluid communication may be controllably interrupted, comprising combining the sample, a reaction buffer, a mixture of free nucleotides and first and second specific oligonucleotide primers in the first reaction chamber and placing the reaction vessel in an automated apparatus such that the automated apparatus heats the first reaction chamber to a sufficient

temperature and for a sufficient time to render any double-stranded first nucleic acid in the sample to be tested into sufficient single-stranded nucleic acid such that a hybridisation product may form, the hybridisation product comprising the first nucleic acid and at least one of the first and second oligonucleotide primers, the automated apparatus then cools the first reaction chamber to a sufficient temperature such that the hybridisation product forms, if the first nucleic acid is present, the automated apparatus then transfers the reaction mixture from the first reaction chamber to the second reaction chamber via the controllable fluid communication such that the reaction mixture is brought into contact with a nucleic acid polymerisation enzyme, the automated apparatus maintains the second reaction chamber at a sufficient temperature which allows for the specific oligonucleotide primer mediated amplification of the first nucleic acid, if present, the automated apparatus then contacts any amplicon product from the first nucleic acid in the second reaction chamber with a capture nucleic acid specific for the amplicon from the first nucleic acid such that a specifically bound nucleic acid-capture probe hybridisation complex may form, the automated apparatus optionally washes the hybridisation complex mixture such that non-specifically bound nucleic acid is washed away from the specifically bound nucleic acid-capture probe complex, the automated apparatus contacts the specifically bound nucleic acid-capture probe complex with a labelled nucleic acid probe specific for the amplicon produced from the first nucleic acid such that a specifically-bound nucleic acid-capture probe-labelled probe complex may form, the automated apparatus optionally washes the specifically bound nucleic acid-capture probe-labelled probe complex such that non-specifically bound labelled probe nucleic acid is washed away from the specifically bound nucleic acid-capture probe-labelled probe complex and the automated apparatus detects the presence or absence of the generated signal and optionally displays a value for the signal, and optionally records a value for the signal, the automated apparatus contacting the specifically-bound nucleic acid-capture probe-labelled probe complex with a solution such that a detectable signal is generated if the amplicon and first nucleic acid are present, the signal generated from the sample being proportional to the amount of the first nucleic acid in the sample, each of the three last steps being performed sequentially or concurrently; (iv) specific automated detection of one or more viral or microbial nucleic acids in a sample comprising lysing at least one microorganism in the sample, if present, to liberate target nucleic acid, amplifying the nucleic acid to form amplicons, contacting the sample with a solid phase receptacle coated with a capture nucleic acid, such that the capture nucleic acid may form a hybridisation complex with the amplicons, allowing the hybridisation complex to form, contacting it with a detection nucleic acid, such that the detection nucleic acid may form a specific hybridisation detection complex with the amplicon, and is conjugated to a means for generating a detectable signal selected from an enzyme, chromophore chemiluminescent compound, radioisotope and fluorophore, allowing the detection complex to form and generating the detectable signal, detecting the detectable signal if the amplicon is present in the sample and optionally, between operations, the hybridisation complex may be washed to remove excess non-specifically bound nucleic acid; (v) a device for the automated detection of a first target nucleic acid and a second target nucleic acid, comprising a solid phase receptacle which is coated with a first capture nucleic acid which may form a specific hybridisation complex with the first nucleic acid and a second capture nucleic acid which may form a specific hybridisation complex with the second nucleic acid; and (vi) automated detection of the presence or absence of a first target nucleic acid and a second target nucleic acid in a sample, comprising contacting the sample with a solid phase receptacle as in (v), allowing a specific hybridisation complex to form if the nucleic acid is present, contacting the solid phase receptacle hybridisation complex with a first detection nucleic acid, which may form a specific hybridisation detection complex with the first nucleic acid and

is conjugated to a means for generating a detectable signal selected from an enzyme, chromophore, chemiluminescent compound, radioisotope and fluorophore, allowing a specific detection complex to form and then generating the detectable signal, detecting the signal if the first nucleic acid is in the sample, contacting the solid phase receptacle hybridisation complex with a second detection nucleic acid which may form a specific hybridisation detection complex with the second nucleic acid and is conjugated to a means for generating a detectable signal selected from enzyme, chromophore, chemiluminescent compound, radioisotope and fluorophore, allowing a specific detection complex to form and then generating the detectable signal, detecting the signal if the second nucleic acid is in the sample, optionally between operations the hybridisation complex being washed to remove excess non-specifically bound nucleic acid and the absence of a detectable signal correlating with the absence of the nucleic acid in the sample.

USE - Process (iv) is useful for detecting Mycobacterium tuberculosis, Chlamydia trachomatis, Neisseria gonorrhoeae or Human Immunodeficiency Virus (HIV) and process (vi) is useful for detecting Chlamydia trachomatis and Neisseria gonorrhoeae.
Dwg.0/30

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L49  ANSWER 91 OF 97  WPIX (C) 2002 THOMSON DERWENT
AN   1998-286851 [25]   WPIX
CR   1998-286850 [25]; 1998-286975 [25]
DNC  C1998-088882
TI   High density immobilisation of thiol-modified nucleic acid on support  -
     derivatised with thiol-reactive group, particularly in arrays for use in
     hybridisation assays, sequencing, synthesis etc., with analysis by mass
     spectrometry, also new apparatus.
DC   B04 D16 J04
IN   CANTOR, C R; KOSTER, H; LITTLE, D P; ODONNELL, M J; O'DONNELL, M; BRAUN,
     A; HILLENKAMP, F; JURINKE, C; KOESTER, H; LOUGH, D M; RUPPERT, A; VAN DEN
     BOOM, D; XIANG, G; O'DONNELL, M J; ODONNELL, M
PA   (SEQU-N) SEQUENOM INC
CYC  80
PI   WO 9820020     A2 19980514 (199825)* EN   156p <--
        RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT
            SD SE SZ UG ZW
         W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
            GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN
            MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ
            VN YU ZW
     AU 9851980     A  19980529 (199841)            <--
     NO 9902169     A  19990706 (199937)            <--
     EP 937096      A2 19990825 (199939)  EN        <--
         R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO
            SE SI
     DE 19782096    T  20000323 (200022)            <--
     DE 29724251    U1 20000817 (200046)            <--
     DE 29724252    U1 20000817 (200046)            <--
     DE 29724341    U1 20001116 (200059)            <--
     DE 29724250    U1 20001019 (200060)            <--
     JP 2001503760 W  20010321 (200122)       189p <--
     EP 1164203     A2 20011219 (200206)  EN        <--
         R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO
            SE SI
     AU 2001076131 A  20020103 (200209)#           <--
     AU 2001091345 A  20020103 (200209)#
     AU 745624      B  20020328 (200235)            <--
ADT  WO 9820020 A2 WO 1997-US20195 19971106; AU 9851980 A AU 1998-51980
     19971106; NO 9902169 A WO 1997-US20195 19971106, NO 1999-2169 19990504; EP
     937096 A2 EP 1997-946893 19971106, WO 1997-US20195 19971106; DE 19782096 T
     DE 1997-19782096 19971106, WO 1997-US20195 19971106; DE 29724251 U1
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Application no. DE 1997-19782096 19971106, DE 1997-29724251 19971106; DE 29724252 U1 Application no. DE 1997-19782096 19971106, DE 1997-29724252 19971106; DE 29724341 U1 Application no. DE 1997-19782096 19971106, DE 1997-29724341 19971106; DE 29724250 U1 Application no. DE 1997-19782096 19971106, DE 1997-29724250 19971106; JP 2001503760 W WO 1997-US20195 19971106, JP 1998-521765 19971106; EP 1164203 A2 Div ex EP 1997-945641 19971106, EP 2001-203019 19971106; AU 2001076131 A Div ex AU 1998-51069 19971106, AU 2001-76131 20010927; AU 2001091345 A Div ex AU 1998-51980 19971106, AU 2001-91345 20011114; AU 745624 B AU 1998-51980 19971106

FDT AU 9851980 A Based on WO 9820020; EP 937096 A2 Based on WO 9820020; DE 19782096 T Based on WO 9820020; JP 2001503760 W Based on WO 9820020; EP 1164203 A2 Div ex EP 954612; AU 2001076131 A Div ex AU 735416; AU 745624 B Previous Publ. AU 9851980, Based on WO 9820020

PRAI **US 1997-947801 19971008; US 1996-746055 19961106 ; US 1997-786988 19970123; US 1997-787639 19970123; US 1996-744481 19961106; US 1996-744590 19961106; US 1996-746036 19961106; US 1997-933792 19970919;** AU 2001-76131 20010927; AU 2001-91345 20011114

AN 1998-286851 [25] WPIX

CR 1998-286850 [25]; 1998-286975 [25]

AB WO 9820020 A UPAB: 20020208

Nucleic acid (I) is immobilised covalently by reacting a thiol-containing (I) with an insoluble support that includes thiol-reactive groups to form a covalent bond.

USE - Supports carrying (I) are used (i) for detecting target (I) by hybridisation; (ii) for solid-phase synthesis of (I); (iii) for sequencing, particularly with analysis by mass spectrometry (MS), e.g. for diagnosis of disease, detection of pathogens and analysis of polymorphisms. The arrays of (7) are used in MS analysis to determine sample composition.

ADVANTAGE - The methods produce sample arrays quickly and provide high density of (I) on the support (at least 12.5 times higher than in previous processes).

Dwg.0/20

L49 ANSWER 92 OF 97 WPIX (C) 2002 THOMSON DERWENT

AN 1997-212892 [19] WPIX

CR 1993-167615 [20]; 1995-185870 [24]; 1996-049867 [05]; 1996-097582 [10]; 1996-171729 [17]; 1998-193778 [17]; 1998-193779 [17]; 1998-333099 [29]; 1998-595120 [50]; 1999-059702 [05]; 1999-069717 [06]; 1999-385567 [32]; 1999-469264 [38]; 1999-527464 [42]; 1999-540606 [45]; 2000-422973 [35]; 2000-442556 [38]; 2001-168473 [12]

DNC C1997-068810

TI Self-addressable and self-assembling system for biological reactions - comprises array of specific binding regions on biochip, also new fluorescence detection system and stringency control device.

DC B04 D16 **J04 S03**

IN HELLER, M J; JACKSON, T R; JUNCOSA, R D; O'CONNELL, J P; SOSNOWSKI, R G; OCONNELL, J P; SOSNOWSKY, R G

PA (NANO-N) NANOGEN INC; (NANO-N) NANOGEN

CYC 25

PI
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WO 9712030     A1 19970403 (199719)* EN   68p <--
   RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
    W: AU BR CA CN JP NZ
AU 9669689     A  19970417 (199732)           <--
EP 852617      A1 19980715 (199832)  EN       <--
    R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 5849486     A  19981215 (199906)           <--
CN 1202929     A  19981223 (199919)           <--
BR 9610618     A  19990406 (199920)           <--
JP 11512605    W  19991102 (200003)       61p <--
NZ 318253      A  20000228 (200017)           <--
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     AU 723134       B  20000817 (200044)          <--
     AU 2000048890 A  20001026 (200059)#          <--
     US 6245508      B1 20010612 (200135)          <--
ADT  WO 9712030 A1 WO 1996-US14353 19960906; AU 9669689 A AU 1996-69689
     19960906; EP 852617 A1 EP 1996-930748 19960906, WO 1996-US14353 19960906;
     US 5849486 A CIP of US 1993-146504 19931101, CIP of US 1994-271882
     19940707, CIP of US 1994-304657 19940909, US 1995-534454 19950927; CN
     1202929 A CN 1996-198521 19960906; BR 9610618 A BR 1996-10618 19960906, WO
     1996-US14353 19960906; JP 11512605 W WO 1996-US14353 19960906, JP
     1997-513452 19960906; NZ 318253 A NZ 1996-318253 19960906, WO 1996-US14353
     19960906; AU 723134 B AU 1996-69689 19960906; AU 2000048890 A Div ex AU
     1996-69689 19960906, AU 2000-48890 20000728; US 6245508 B1 CIP of US
     1993-146504 19931101, CIP of US 1994-271882 19940707, CIP of US
     1994-304657 19940909, Cont of US 1995-534454 19950927, US 1998-141286
     19980827
FDT  AU 9669689 A Based on WO 9712030; EP 852617 A1 Based on WO 9712030; US
     5849486 A CIP of US 5605662, CIP of US 5632957; BR 9610618 A Based on WO
     9712030; JP 11512605 W Based on WO 9712030; NZ 318253 A Based on WO
     9712030; AU 723134 B Previous Publ. AU 9669689, Based on WO 9712030; AU
     2000048890 A Div ex AU 723134; US 6245508 B1 CIP of US 5605662, CIP of US
     5632957, Cont of US 5849486, CIP of US 6017696
PRAI US 1995-534454    19950927; US 1993-146504    19931101
     ; US 1994-271882    19940707; US 1994-304657
     19940909; AU 2000-48890    20000728; US
     1998-141286    19980827
AN   1997-212892 [19]    WPIX
CR   1993-167615 [20]; 1995-185870 [24]; 1996-049867 [05]; 1996-097582 [10];
     1996-171729 [17]; 1998-193778 [17]; 1998-193779 [17]; 1998-333099 [29];
     1998-595120 [50]; 1999-059702 [05]; 1999-069717 [06]; 1999-385567 [32];
     1999-469264 [38]; 1999-527464 [42]; 1999-540606 [45]; 2000-422973 [35];
     2000-442556 [38]; 2001-168473 [12]
AB   WO    9712030 A UPAB: 20020711
     Apparatus for enhanced detection of a biological reaction between a sample
     and an active area of a biochip, comprises the biochip and a fluidic
     system designed to pass the sample over the active area.
          USE - The methods can be used for diagnosis, analysis and
     multistep/multiplex reactions (including synthesis of biopolymers),
     especially those involving nucleic acid hybridisation (but also
     antigen-antibody reactions).
          ADVANTAGE - Use of a flow system improves diagnostic efficiency,
     allows more complete sampling and the detection device provides imaging of
     very small volumes. Together these elements provide a highly automated DNA
     analysis system from self-addressable and self-assembling electronic
     components. The DNA fingerprinting method allows the length of the
     hybridising fragments to be determined, and reversing the polarity of the
     reaction sites improves specificity by releasing any unbound analyte or
     reagent.
     Dwg.2A/16

L49  ANSWER 93 OF 97  WPIX (C) 2002 THOMSON DERWENT
AN   1995-329307 [43]    WPIX
DNC  C1995-146076
TI   Processing of nucleic acids at a temp. regulated surface - partic. rapid
     amplification and detection in an otherwise isothermal reaction mixt..
DC   B04 D16
IN   BERTLING, W
PA   (BOEF) BOEHRINGER MANNHEIM GMBH
CYC  19
PI   DE 4409436      A1 19950921 (199543)*       10p <--
     WO 9525592      A1 19950928 (199544)  DE    35p <--
        RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
         W: JP US
     EP 751827       A1 19970108 (199707)  DE        <--
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R: AT CH DE ES FR GB IT LI
JP 09510353 W 19971021 (199801) 33p <--
EP 751827 B1 19980819 (199837) DE <--
R: AT CH DE ES FR GB IT LI
DE 59503269 G 19980924 (199844) <--
ES 2123239 T3 19990101 (199907) <--
US 5985555 A 19991116 (200001) <--

ADT DE 4409436 A1 DE 1994-4409436 19940319; WO 9525592 A1 WO 1995-EP975 19950316; EP 751827 A1 EP 1995-913132 19950316, WO 1995-EP975 19950316; JP 09510353 W JP 1995-524364 19950316, WO 1995-EP975 19950316; EP 751827 B1 EP 1995-913132 19950316, WO 1995-EP975 19950316; DE 59503269 G DE 1995-503269 19950316, EP 1995-913132 19950316, WO 1995-EP975 19950316; ES 2123239 T3 EP 1995-913132 19950316; US 5985555 A WO 1995-EP975 19950316, US 1996-704682 19960919

FDT EP 751827 A1 Based on WO 9525592; JP 09510353 W Based on WO 9525592; EP 751827 B1 Based on WO 9525592; DE 59503269 G Based on EP 751827, Based on WO 9525592; ES 2123239 T3 Based on EP 751827; US 5985555 A Based on WO 9525592

PRAI **DE 1994-4409436 19940319**

AN 1995-329307 [43] WPIX

AB DE 4409436 A UPAB: 19951102
Processing of nucleic acids (I) in a reaction mixt. comprises regulating the temp. at the mixt. surface (and in its immediate surroundings) while a part of the mixt. remains under practically isothermal conditions.

Also new is a device for carrying out this process.

USE - The method is partic. used in diagnostic amplification and/or detection processes, but can also be used e.g. to enrich specific (I) through hybridisation, to transfer (I) between solns. and for sequencing.

ADVANTAGE - The method can be applied to reaction vols. of any size and only needs very short processing times as the heating and cooling are only applied to a small part of the total reaction vol.. The reagents used need not have a high stability to heat, e.g. it may be possible to use non-heat stable polymerases.
Dwg.1/3

L49 ANSWER 94 OF 97 WPIX (C) 2002 THOMSON DERWENT
AN 1995-224283 [29] WPIX
CR 1997-099909 [09]; 1999-527007 [44]; 2000-430224 [35]
DNN N1995-175825 DNC C1995-103174
TI Single stranded nucleic acids contg. electron donor and acceptor moieties - useful as bio-conductors and diagnostic probes.
DC B04 D16 **S03**
IN FRASER, S E; KAYYEM, J F; MEADE, T J
PA (CALY) CALIFORNIA INST OF TECHNOLOGY; (CALY) CALIFORNIA INST OF TECHN
CYC 60
PI WO 9515971 A2 19950615 (199529)* EN 59p <--
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA UZ VN
AU 9512152 A 19950627 (199541) <--
WO 9515971 A3 19950803 (199619) <--
EP 733058 A1 19960925 (199643) EN <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5591578 A 19970107 (199708) 18p <--
JP 09506510 W 19970630 (199736) 58p <--
US 5705348 A 19980106 (199808) 22p <--
US 5770369 A 19980623 (199832) <--
US 5780234 A 19980714 (199835) <--
AU 703329 B 19990325 (199924) <--
US 6087100 A 20000711 (200037) <--
US 6177250 B1 20010123 (200107) <--
US 6180352 B1 20010130 (200108) <--

US 6200761 B1 20010313 (200120) <--
US 6238870 B1 20010529 (200132) <--
US 6258545 B1 20010710 (200141) <--
US 6268149 B1 20010731 (200146) <--
US 6268150 B1 20010731 (200146) <--
US 6277576 B1 20010821 (200150) <--
US 2001034033 A1 20011025 (200170) <--
US 2001046679 A1 20011129 (200202) <--
EP 1172446 A2 20020116 (200207) EN <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 733058 B1 20020410 (200227) EN <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69430384 E 20020516 (200240) <--

ADT WO 9515971 A2 WO 1994-US13893 19941205; AU 9512152 A AU 1995-12152 19941205; EP 733058 A1 WO 1994-US13893 19941205, EP 1995-903194 19941205; US 5591578 A US 1993-166036 19931210; JP 09506510 W WO 1994-US13893 19941205, JP 1995-516249 19941205; US 5705348 A Cont of US 1993-166036 19931210, US 1996-709265 19960906; US 5770369 A Cont of US 1993-166036 19931210, Cont of US 1995-475051 19950607, US 1996-660534 19960607; US 5780234 A Cont of US 1993-166036 19931210, US 1996-709263 19960906; AU 703329 B AU 1995-12152 19941205; US 6087100 A Cont of US 1993-166036 19931210, Cont of US 1996-709263 19960906, US 1997-946679 19971008; US 6177250 B1 Cont of US 1993-166036 19931210, Cont of US 1995-475051 19950607, Cont of US 1996-660534 19960607, US 1999-306737 19990507; US 6180352 B1 Cont of US 1993-166036 19931210, Cont of US 1995-475051 19950607, Cont of US 1996-660534 19960607, Cont of US 1997-873598 19970612, Cont of US 1999-306749 19990507, US 1999-459191 19991210; US 6200761 B1 Cont of US 1993-166036 19931210, Cont of US 1995-475051 19950607, Cont of US 1996-660534 19960607, Cont of US 1997-873598 19970612, Cont of US 1999-306749 19990507, US 1999-454497 19991206; US 6238870 B1 Cont of US 1993-166036 19931210, Cont of US 1995-475051 19950607, Cont of US 1996-660534 19960607, Cont of US 1997-873598 19970612, Cont of US 1999-306749 19990507, US 1999-458187 19991208; US 6258545 B1 Cont of US 1993-166036 19931210, Cont of US 1995-475051 19950607, Cont of US 1996-660534 19960607, Cont of US 1998-100507 19980619, US 2000-545227 20000407; US 6268149 B1 Cont of US 1993-166036 19931210, Cont of US 1996-709263 19960906, Cont of US 1997-946679 19971008, US 1999-454498 19991206; US 6268150 B1 Cont of US 1993-166036 19931210, Cont of US 1995-475051 19950607, Cont of US 1996-660534 19960607, Cont of US 1997-873598 19970612, Cont of US 1999-306749 19990507, US 1999-459751 19991210; US 6277576 B1 Cont of US 1993-166036 19931210, Cont of US 1995-475051 19950607, Cont of US 1996-660534 19960607, Cont of US 1997-873598 19970612, US 1999-306768 19990507; US 2001034033 A1 Cont of US 1993-166036 19931210, Cont of US 1996-709263 19960906, Cont of US 1997-946679 19971008, Cont of US 1999-454498 19991206, US 2001-866067 20010523; US 2001046679 A1 Cont of US 1993-166036 19931210, Cont of US 1995-475051 19950607, Cont of US 1996-660534 19960607, Cont of US 1998-100507 19980619, Cont of US 2000-545227 20000407, US 2001-845746 20010430; EP 1172446 A2 Div ex EP 1995-903194 19941205, EP 2001-122329 19941205; EP 733058 B1 WO 1994-US13893 19941205, EP 1995-903194 19941205, Related to EP 2001-122329 19941205; DE 69430384 E DE 1994-630384 19941205, WO 1994-US13893 19941205, EP 1995-903194 19941205

FDT AU 9512152 A Based on WO 9515971; EP 733058 A1 Based on WO 9515971; JP 09506510 W Based on WO 9515971; US 5705348 A Cont of US 5591578; US 5770369 A Cont of US 5591578; US 5780234 A Cont of US 5591578; AU 703329 B Previous Publ. AU 9512152, Based on WO 9515971; US 6087100 A Cont of US 5591578, Cont of US 5780234; US 6177250 B1 Cont of US 5591578, Cont of US 5770369, Cont of US 5824473; US 6180352 B1 Cont of US 5591578, Cont of US 5770369, Cont of US 5824473, Cont of US 5952172; US 6200761 B1 Cont of US 5591578, Cont of US 5770369, Cont of US 5824473, Cont of US 5952172; US 6238870 B1 Cont of US 5591578, Cont of US 5770369, Cont of US 5824473, Cont of US 5952172; US 6258545 B1 Cont of US 5591578, Cont of US 5770369, Cont of US 5824473, Cont of US 6071699; US 6268149 B1 Cont of US 5591578,

Cont of US 5780234, Cont of US 6087100; US 6268150 B1 Cont of US 5591578, Cont of US 5770369, Cont of US 5824473, Cont of US 5952172; US 6277576 B1 Cont of US 5591578, Cont of US 5770369, Cont of US 5824473, Cont of US 5952172; US 2001034033 A1 Cont of US 5591578, Cont of US 5780234, Cont of US 6087100, Cont of US 6268149; US 2001046679 A1 Cont of US 5591578, Cont of US 5770369, Cont of US 5824473, Cont of US 6071699, Cont of US 6258545; EP 1172446 A2 Div ex EP 733058; EP 733058 B1 Related to EP 1172446, Based on WO 9515971; DE 69430384 E Based on EP 733058, Based on WO 9515971

PRAI **US 1993-166036 19931210; US 1996-709265 19960906 ; US 1995-475051 19950607; US 1996-660534 19960607; US 1996-709263 19960906; US 1997-946679 19971008; US 1999-306737 19990507; US 1997-873598 19970612; US 1999-306749 19990507 ; US 1999-459191 19991210; US 1999-454497 19991206; US 1999-458187 19991208; US 1998-100507 19980619; US 2000-545227 20000407; US 1999-454498 19991206; US 1999-459751 19991210 ; US 1999-306768 19990507;** US 2001-866067 20010523; US 2001-845746 20010430

AN 1995-224283 [29] WPIX

CR 1997-099909 [09]; 1999-527007 [44]; 2000-430224 [35]

AB WO 9515971 A UPAB: 20020626

A single stranded (ss) nucleic acid (NA) contains at least 1 electron donor moiety and at least 1 electron acceptor moiety, both being covalently attached to the NA. Also claimed are: (1) a compsn. comprising first and second ss NA's as above, where the donor and acceptor are covalently linked to the ribose-phosphate backbone; (2) a double-stranded (ds) NA compsn. where the first ss NA is hybridised to the second NA; (3) prepn. of a ss NA contg. an electron transfer moiety at the 5' end;(4) prepn. of a ss NA contg. an electron transfer moiety covalently attached to an internal nucleotide by incorporating a modified nucleotide dimer into the growing NA to form a modified ss NA; (5) prepn. of a ss NA contg. an electron transfer moiety covalently attached to the 3' terminal;(6) detecting a target sequence in a NA sample by: (a) hybridising a ss NA contg. at least 1 covalently attached electron donor and acceptor moiety to the target sequence to form a hybridisation complex; (b) determining the electron transfer rate between the donor and acceptor in the complex, and (c) comparing the rate with that in the absence of the target sequence as an indicator of the presence/absence of the target; and (7) detecting a target sequence in a NA sample where the target comprises adjacent first and second target domains.

USE - The addn. of the electron donor and acceptor moieties allows selective modification of NAs at specific sites to form complexes that are biomolecular templates capable of transferring electrons over very large distances at extremely fast rates. Their unique structure enables their use as a new class of bioconductors and diagnostic probes. The probes are useful in mol. biology and diagnostic medicine. They are extremely specific and sensitive. The methods allow the detection of base pain mismatches.

Dwg.0/4

ABEQ US 5591578 A UPAB: 19970220

A single-stranded nucleic acid containing one or multiple electron donor moieties and one or multiple electron acceptor moieties, wherein said electron donor and acceptor moieties are transition metal complexes covalently attached to the 2' or 3' position of a ribose of the ribose-phosphate backbone of said nucleic acid, said transition metal selected from the group consisting of Cd, Mg, Cu, Co, Pd, Zn, Fe and Ru, and wherein electron transfer can occur between said electron donor and acceptor moieties when said single stranded nucleic acid is hybridized to a target sequence.

Dwg.0/4

ABEQ US 5705348 A UPAB: 19980223

A single stranded (ss) nucleic acid (NA) contains at least 1 electron

donor moiety and at least 1 electron acceptor moiety, both being covalently attached to the NA. Also claimed are: (1) a compsn. comprising first and second ss NA's as above, where the donor and acceptor are covalently linked to the ribose-phosphate backbone; (2) a double-stranded (ds) NA compsn. where the first ss NA is hybridised to the second NA; (3) prepn. of a ss NA contg. an electron transfer moiety at the 5' end;(4) prepn. of a ss NA contg. an electron transfer moiety covalently attached to an internal nucleotide by incorporating a modified nucleotide dimer into the growing NA to form a modified ss NA; (5) prepn. of a ss NA contg. an electron transfer moiety covalently attached to the 3' terminal;(6) detecting a target sequence in a NA sample by: (a) hybridising a ss NA contg. at least 1 covalently attached electron donor and acceptor moiety to the target sequence to form a hybridisation complex; (b) determining the electron transfer rate between the donor and acceptor in the complex, and (c) comparing the rate with that in the absence of the target sequence as an indicator of the presence/absence of the target; and (7) detecting a target sequence in a NA sample where the target comprises adjacent first and second target domains.

USE - The addn. of the electron donor and acceptor moieties allows selective modification of NAs at specific sites to form complexes that are biomolecular templates capable of transferring electrons over very large distances at extremely fast rates. Their unique structure enables their use as a new class of bioconductors and diagnostic probes. The probes are useful in mol. biology and diagnostic medicine. They are extremely specific and sensitive. The methods allow the detection of base pain mismatches.

Dwg.0/4

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L49  ANSWER 95 OF 97  WPIX (C) 2002 THOMSON DERWENT
AN   1994-200296 [24]   WPIX
DNC  C1994-091596
TI   Process for genotyping Hepatitis C virus (HCV) isolates - utilises probes
     hybridising to HCV isolate domains.
DC   B04 D16
IN   MAERTENS, G; ROSSAU, R; STUYVER, L; VAN HEUVERSWYN, H
PA   (INNO-N) INNOGENETICS NV SA; (INNO-N) INNOGENETICS NV
CYC  48
PI   WO 9412670     A2 19940609 (199424)* EN   96p <--
        RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
         W: AT AU BB BG BR BY CA CH CZ DE DK ES FI GB HU JP KP KR KZ LK LU LV
            MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US UZ VN
     AU 9456282     A  19940622 (199436)            <--
     EP 637342      A1 19950208 (199510)  EN        <--
         R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
     WO 9412670     A3 19940721 (199517)            <--
     JP 07503143    W  19950406 (199522)            <--
     AU 681612      B  19970904 (199744)            <--
     SG 46456       A1 19980220 (199822)            <--
     US 5846704     A  19981208 (199905)            <--
     EP 905258      A2 19990331 (199917)  EN        <--
         R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
     EP 637342      B1 19990428 (199921)  EN        <--
         R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
     DE 69324678    E  19990602 (199928)            <--
     ES 2133529     T3 19990916 (199946)            <--
     US 6051696     A  20000418 (200026)            <--
     US 6171784     B1 20010109 (200104)            <--
     EP 1197568     A2 20020417 (200233)  EN        <--
         R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
ADT  WO 9412670 A2 WO 1993-EP3325 19931126; AU 9456282 A AU 1994-56282
     19931126; EP 637342 A1 WO 1993-EP3325 19931126, EP 1994-901891 19931126;
     WO 9412670 A3 WO 1993-EP3325 19931126; JP 07503143 W WO 1993-EP3325
     19931126, JP 1994-512767 19931126; AU 681612 B AU 1994-56282 19931126; SG
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46456 A1 SG 1996-4862 19931126; US 5846704 A WO 1993-EP3325 19931126, US 1994-256568 19940718; EP 905258 A2 Div ex EP 1994-901891 19931126, EP 1998-117538 19931126; EP 637342 B1 WO 1993-EP3325 19931126, EP 1994-901891 19931126, Related to EP 1998-117538 19931126; DE 69324678 E DE 1993-624678 19931126, WO 1993-EP3325 19931126, EP 1994-901891 19931126; ES 2133529 T3 EP 1994-901891 19931126; US 6051696 A Div ex WO 1993-EP3325 19931126, Div ex US 1994-256568 19940718, US 1998-44665 19980319; US 6171784 B1 Cont of WO 1993-EP3325 19931126, Cont of US 1994-256568 19940718, US 1998-38369 19980310; EP 1197568 A2 Div ex EP 1994-901891 19931126, Div ex EP 1998-117538 19931126, EP 2001-121347 19931126

FDT AU 9456282 A Based on WO 9412670; EP 637342 A1 Based on WO 9412670; JP 07503143 W Based on WO 9412670; AU 681612 B Previous Publ. AU 9456282, Based on WO 9412670; US 5846704 A Based on WO 9412670; EP 905258 A2 Div ex EP 637342; EP 637342 B1 Related to EP 905258, Based on WO 9412670; DE 69324678 E Based on EP 637342, Based on WO 9412670; ES 2133529 T3 Based on EP 637342; US 6171784 B1 Cont of US 5846704; EP 1197568 A2 Div ex EP 637342, Div ex EP 905258

PRAI **EP 1993-402129 19930831; EP 1992-403222 19921127**

AN 1994-200296 [24] WPIX

AB WO 9412670 A UPAB: 20010207

A process for genotyping hepatitis C virus (HCV) isolates in biological samples comprises: (a) contacting the sample, in which ribo- or deoxyribonucleotides have been made accessible opt. under denaturation, with a probe which is either (i) capable of hybridising to a region in the domain from position -291 to -66 of the 5'-untranslated region of an HCV isolate, or (ii) complementary to (i); and (b) detecting the complexes formed between the probe and HCV isolate nucleotide sequence.

USE/ADVANTAGE - The probes are useful for genotyping HCV isolates as belonging to the HCV types- HCV type 2, type 3, type 4, type 5 or type 6, and subtypes of these e.g. 1a, 1b, 2a, 2b, 2c, 3a, 3b, 3c, 4a, 4b, 4c, 4d, 4e, 4f, 4g and 4h. The process can be utilised to simultaneously genotype all HCV isolates in a biological sample (claimed).

Dwg.0/10

L49 ANSWER 96 OF 97 WPIX (C) 2002 THOMSON DERWENT

AN 1994-147008 [18] WPIX

DNC C1994-067156

TI Detection of a lactobacillus genus microbe - by using PCR amplification of a gene in the 16S-23S rRNA gene space.

DC B04 D16

PA (TAKI) TAKARA SHUZO CO LTD

CYC 1

PI JP 06090793 A 19940405 (199418)* 14p <--
JP 3107904 B2 20001113 (200060) 18p <--

ADT JP 06090793 A JP 1992-113154 19920407; JP 3107904 B2 JP 1992-113154 19920407

FDT JP 3107904 B2 Previous Publ. JP 06090793

PRAI **JP 1992-113154 19920407**

AN 1994-147008 [18] WPIX

AB JP 06090793 A UPAB: 19940622

A method for the detection of a Lactobacillus genus microbe in which a gene (I) in the spacer region between the gene coding 16S rRNA and the gene coding 23S rRNA of a L. genus microbe is detected.

Also claimed are the above gene (I) in the spacer region and a kit for the detection of a L. genus microbe contg. a specific primer for the amplification of (I).

USE/ADVANTAGE - The method can detect a L. genus microbe, particularly a Hiochi microbe, rapidly in a high sensitivity.

Dwg.0/0

L49 ANSWER 97 OF 97 WPIX (C) 2002 THOMSON DERWENT

AN 1984-088272 [14] WPIX

DNN N1984-065969 DNC C1984-037652

L27	13	S L26 AND L23
L28	8	S L23 NOT L27
		SEL DN AN 4
L29	1	S L28 AND E42-E44
L30	14	S L27,L29
L31	1051	S L26 AND L5
L32	1018	S L31 AND C12M001-34/IC,ICM
L33	87	S L32 AND L8
L34	86	S L33 NOT L18
L35	40	S L32 AND G06F/IC,ICM,ICS,ICA,ICI
L36	5	S L33 AND L35
L37	19	S L30,L36
L38	35	S L35 NOT L37
L39	81	S L34 NOT L35-L38
L40	100	S L37,L39
L41	39	S L40 AND PY<=2000
L42	99	S L40 AND PRY<=2000
L43	99	S L41,L42
L44	92	S L43 AND C12M/IC,ICM,ICS
L45	7	S L43 NOT L44
L46	6	S L45 NOT ASSEMBLY/TI
L47	91	S L44 NOT PICOLIT?/PA
L48	91	S L44 NOT (ELLSON R? OR MUTZ M? OR HARRIS D?)/AU
L49	97	S L46,L47,L48

FILE 'WPIX' ENTERED AT 14:29:24 ON 13 AUG 2002